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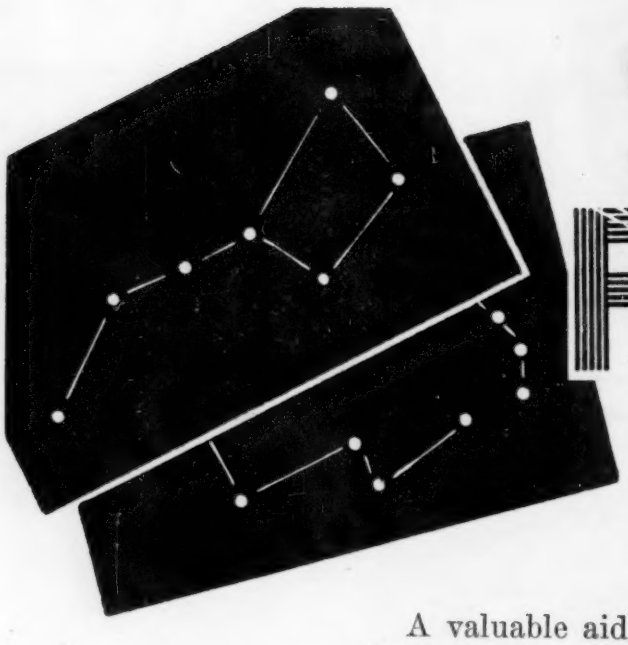
SCIENCE

James Graham Chesnutt who won the $1,000 AAAS–George Westinghouse Science Writing Award for Newspapers as announced last week in *Science*. Mr. Chesnutt will be present at a luncheon in Boston 27 December to receive the award and a citation for accurate and readable scientific news reporting. The winning story, describing the work of Karl F. Meyer, director of the Hooper Foundation for Medical Research, University of California, on chemotherapy of Bubonic Plague, appeared in the *Call-Bulletin*, San Francisco, where Mr. Chesnutt is employed as a reporter and rewrite man. He was discharged from the Army last Spring with the rank of Lieutenant-Colonel after having been with the Psychological Warfare Branch, SHAEF. After VE day he helped to reorganize the German press.

Genes and Nucleoproteins in the Synthesis of Enzymes

S. Spiegelman and M. D. Kamen



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SCIENCE

Vol. 104, No. 2712 Friday, 20 December 1946

Genes and Nucleoproteins in the Synthesis of Enzymes[1]

S. Spiegelman and M. D. Kamen

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PREVIOUS PUBLICATIONS (*14, 16*) reported examinations of substrate-induced enzyme formation in genetically controlled yeast strains in an attempt to employ this phenomenon as a tool for the analysis of the gene-enzyme relationship problem. Some of the pertinent facts which emerged from these studies may be summarized briefly as follows: (1) Potentiality for enzyme formation can segregate in a Mendelian fashion; (2) substrates, rather than genes, critically control enzyme activity levels; and (3) an enzyme (melibiase) can be maintained in the presence of substrate for an indefinite number of cell generations in the absence of the gene necessary to the initiation of its synthesis.

These findings suggested the existence of a cytoplasmic self-duplicating entity as being involved in enzyme synthesis. Whether the entity was the enzyme itself or something mediating its formation could not be decided on the basis of the observations. However, because of its simplicity the former was adopted as a tentative working hypothesis. In any case, it was evident that, in so far as enzymatic constitution was concerned, the cytoplasm possessed a degree of autonomy from the genome not easily reconcilable with the more classical views of gene-enzyme relationships in which the gene is considered as the only self-duplicating unit in the cell.

Subsequent experiments were designed to obtain more information on the mechanism of enzyme formation with particular reference to energy requirements. It is proposed to report here certain of the results obtained as being particularly suggestive for the gene-enzyme problem and to discuss their implications.

It has been found (*15*) that enzyme synthesis under anaerobic conditions could be prevented either with NaN_3 or dinitrophenol without disturbing the rate of carbohydrate metabolism. The ability of these substances to prevent utilization of metabolic energy for synthetic activity is apparently quite general, having been demonstrated for such diverse processes as cell division (*8*), carbohydrate and ammonia assimilation (*18*), and cell regeneration (*9*).

On the assumption that phosphate-bond energy, as generated by the glycolytic system, forms the primary source of energy for cell function and growth under anaerobic conditions, experiments were undertaken to examine the effect of these agents on phosphorus metabolism, using radioactive phosphorus (P^{32}) as a tracer.

The most consistent correlation between phosphorus metabolism and protein or enzyme formation was found in the flow of phosphate *from* the nucleoprotein fraction (NP). This latter is the residue phosphate remaining after successive extractions with water, cold trichloroacetic acid, alcohol, and hot alcohol-ether (3:1).

The behavior of the phosphate in this fraction was followed under various conditions, employing P^{32} in the following manner: Cells were grown in the usual media at 30° C. in the presence of P^{32} (activity, 5×10^5 cts./min./mg. P). This resulted in complete equilibration of the labeled phosphorus in all fractions. After 48 hours these cells were harvested, washed three times in unlabeled M/15 KH_2PO_4, resuspended in unlabeled M/15 KH_2PO_4 with 4 per cent glucose, and allowed to ferment the carbohydrate under completely anaerobic conditions. No budding or increase in protein nitrogen is observed in such suspensions. Samples were withdrawn at intervals for activity measurements. It was found that within 4 hours about half of the total activity was lost. After fractionation it was found that (except for 1 or 2 per cent) this loss in activity could be completely accounted for in the acid-soluble fraction which forms about 50 per cent of the total P content of the cells. The total activity (P^{32} content) as well as total P^{31} of the nucleoprotein fraction had actually increased slightly (8 per cent) during this period, indicating flow of phosphate into this fraction. These data clearly showed that rapidly metabolizing but nondividing cells did not lose phosphate from the NP fraction even though the major portion of the remaining phosphate

[1] Aided by a grant from the International Cancer Research Foundation.

was being rapidly equilibrated. Since activity of the phosphate in the acid-soluble fraction of such cells was about one-fourth that of the NP phosphate, they were favorable material for the further study of exchanges between the two fractions. Allowing such cells to ferment carbohydrate for longer periods of time (up to 6 hours) again left the *total* activity of the NP fraction unchanged, although the specific activity was decreased due to dilution by the flow of low specific activity phosphate from the acid-soluble fraction.

The entire behavior of the NP fraction was changed, however, when such cells were induced to synthesize new protein either by adding ammonia or by forcing the synthesis of a new enzyme. The results obtained in a typical experiment are exemplified by the data

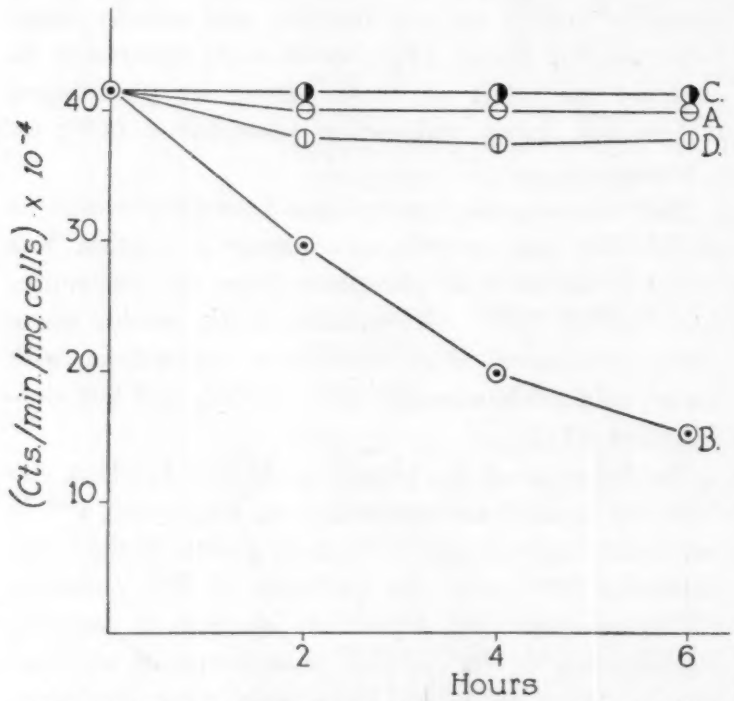


FIG. 1. Behavior of NP phosphate when new protein is being synthesized (B) and when protein formation is prevented by absence of nitrogen supply (A), presence of sodium azide (C), or dinitrophenol (D).

in Fig. 1. In this experiment cells were suspended in physiological saline[2] containing: (a) glucose, (b) glucose + $(NH_4)_2SO_4$, (c) glucose + $(NH_4)_2SO_4$ + NaN_3, (d) glucose + $(NH_4)_2SO_4$ + dinitrophenol. The amount of $(NH_4)_2SO_4$ was equivalent in nitrogen to 50 per cent of the nitrogen content of the yeast. The concentrations of NaN_3 and dinitrophenol were 5×10^{-3} and 5×10^{-4} M, respectively—sufficient to completely inhibit enzyme formation.

It will be noted that with glucose alone there was no change in activity, whereas when ammonia was present, with consequent budding, the nucleoprotein P dropped to 38 per cent of its original total activity, indicating a flow of phosphate from this fraction. It is evident that the azide and, to only a slightly lesser extent, the dinitrophenol were able to prevent this utilization. Except for the fact that the transfer of less phosphate was involved, the same phenomenon was observed when cells were induced to form a new enzyme. Thus, in an experiment in which cells were adapted to maltose, a 34-per cent drop in activity of the nucleoprotein phosphate was observed. Again azide and dinitrophenol in the above concentrations prevented both the formation of the enzyme and the transfer of phosphate from the NP fraction.

These findings provide us with the following correlations between protein or enzyme synthesis and the transfer of phosphate from the NP fraction: (1) Rapidly metabolizing cells which are not synthesizing new protein do not transfer phosphate from the NP fraction; (2) synthesis of new protein or enzyme is paralleled by a marked transfer of phosphate from the NP fraction; (3) agents which are effective in inhibiting enzyme formation and protein synthesis also prevent flow of P from the NP fraction. To these must be added the fundamental observations of Caspersson and his collaborators on yeast (*2*), as well as many other cells, which point to a rigid connection between nucleic acid metabolism and protein synthesis.

In the light of the data presented here, which introduce nucleoproteins as controlling elements in enzyme synthesis, it seems highly desirable to reexamine our previous experiments and interpretations. Several problems are raised, among them the function performed by the nucleoprotein and, closely related, the nature of the relation of the nucleoprotein to the gene, on the one hand, and to the enzyme whose formation it mediates, on the other. An obvious opportunity exists here for a rational linkage of these three fundamental units.

Modern biochemical research (*7*) which has emphasized the role of organic phosphate bonds as sources of energy for synthetic activities provides a foundation upon which may be based a reasonable hypothesis of nucleoprotein function in enzyme synthesis. Of particular value here is the mechanism of complex polysaccharide synthesis, the elucidation of which we owe to the work of the Coris (*3*) and their collaborators. It is found that in the synthesis of a glycosidic bond, glucose-1-phosphate rather than glucose is the reactant involved. The unique feature here is the conversion of an energy-requiring synthetic step into a spontaneous reaction by supplying the necessary energy *in the molecular structure of one of the reactants.*

From this it would appear that the quantitative energy requirement for a particular synthetic reaction is not the crucial issue. There are many phosphory-

[2] The use of exogenous inorganic phosphate decreases quantitatively the flow of phosphate from the NP fraction as observed by activity measurements, since there is a tendency for the cells to utilize the more recently esterified phosphate for synthetic purposes.

lated compounds (e.g. glucose-6-phosphate, adenosinetriphosphate) which have more than sufficient energy to form a glycosidic link if there actually existed some mechanism for 'feeding' it into the reaction. However, the energy content of these compounds cannot be used for this purpose. Clearly, a further requirement is what may be called "specificity" of bond energy. Thus, the actual nature of the bond, and the compound carrying the energy, will determine its suitability for driving a particular reaction. The energy generated by the 'catabolic wheel' and trapped in such energy accumulators as adenosinetriphosphate or creatine-phosphate is too 'generalized' to be used in driving the various synthetic mechanism of anabolism. The energy contained in such compounds must be transferred to others which can act as specific energy donators for particular synthetic reactions.

This concept unifies and simplifies the problem of biological synthesis, since it avoids separating the problem of synthesis into one involving the reactants and another concerned with the source of the "coupled" driving energy.

From this point of view it is not surprising to find that nucleoproteins are controlling elements in protein formation. We may further plausibly suggest that these phosphorus-containing proteins are the specific energy donators which make possible reactions leading to protein and enzyme synthesis.[3]

It would be hazardous at present to attempt to offer a definitive formulation of what we mean by a 'self-duplicating' unit. However, one attribute it is likely to possess is the ability to transform and accumulate energy within its own molecular structure which can be used for the synthesis of similar units. At any rate, it is relatively easy to show that the growth kinetics of such 'energy accumulators' is of the self-duplicating or autocatalytic type. Of the known proteins, those containing phosphorus would be the most likely to possess this property.

In the light of the data presented here and the above discussion it seems reasonable to adopt the tentative working hypothesis that the cytoplasmic self-duplicating entities previously found (*14, 16*) to be involved in enzyme formation are nucleoproteins rather than the enzyme itself. Such an hypothesis would be in harmony with the findings that all accepted self-duplicating units (with but one or two isolated exceptions) have been found to be inseparably linked with nucleic acid-containing compounds. Among such entities may be mentioned genes (*12*), plastogenes (*19*), viruses (*5*), and the pneumococcus 'transforming principle' (*1*).

[3] H. J. Muller (personal communication) independently suggested that nucleoproteins might provide the energy for protein synthesis in his Pilgrim Lecture in London, November 1945 (in press).

From the assumption that the nucleoprotein rather than the enzyme is the cytoplasmic self-duplicating unit several experimental consequences follow. It would be expected that cells not possessing the initiating gene for a particular enzyme could still retain capacity for synthesis of such an enzyme, even in the absence of this enzyme, providing an adequate number of nucleoprotein units were present. Experiments with melibiase (*16*) are consistent with this point of view. In some of the clones missing the mel + gene, irreversible loss of potentiality for melibiase synthesis was not obtained until about 20 hours subsequent to the disappearance of all measurable enzyme. Thus, for a considerable period of time these cells retained the capacity for the synthesis of this enzyme in the absence of any evidence for its presence in the cytoplasm. Recent experiments (*6*), suggesting that cytoplasmic transmission of the capacity to form enzyme can occur in the absence of any measurable enzyme activity, would also support this idea.

In view of the presumed chemical similarity between the two, it seems almost necessary to conclude that the self-duplicating nucleoprotein which mediates protein and enzyme formation is derived from the gene. The value of this conclusion resides in the fact that it provides us with an experimentally analyzable entity which can bridge the gap between the gene in the nucleus and the enzyme in the cytoplasm.

We are thus led to propose the following concept of gene action: Genes *continually* produce at different rates partial replicas of themselves which enter the cytoplasm. These replicas are nucleoprotein in nature and possess to varying degrees the capacity for self-duplication. Their presence in the cytoplasm controls the type and amounts of proteins and enzymes synthesized. These cytoplasmic self-duplicating units, like all such entities, would compete with each other, and the outcome of such competitive interaction would then determine the enzymatic make-up of the cytoplasm. Inherent in this concept is the possibility of changing the ultimate result of this competition by varying the conditions under which it takes place.

The unique feature of this kind of theory is that while supplying a link between gene and enzyme it at the same time predicts that cells with identical genomes need not possess identical enzymatic constitutions. Whether a particular character will be transmitted from one cell generation to the next in a Mendelian fashion will, thus, depend on the relative rates of duplication of the controlling cytoplasmic units as compared with their rate of production from the gene. If the latter is quantitatively determining, Mendelian inheritance will be observed; if the former is determining, the Mendelian picture will be obscured to varying degrees. As a tentative working hypothesis, it has

the advantage of providing a unified point of view from which such diverse and apparently contradictory phenomena as classical Mendelian genetics, cytoplasmic inheritance, cellular differentiation, and enzymatic adaptation may be analyzed.

The basic problem of cancer involves explaining the appearance of a sudden *heritable* change in somatic cells analogous in several ways to enzyme adaptation or cellular differentiation. It is, therefore, not surprising that cancer investigators (*11, 17, 20*) were one of the first groups of biological workers to strongly support the suggested existence of a cytoplasmic hereditary unit. An entity of this kind, by being self-duplicating, provides them with another level at which a mutation can take place and be subsequently transmitted via the cytoplasm from one cell generation to the next.

More or less similar views have been proposed by geneticists. Wright (*21*) in particular emphasized several difficulties in trying to explain either growth or differentiation in terms of the classical Mendelian concept of the gene. Thus, assumption that every time a new protein molecule is formed during growth the gene on the chromosome must intervene as a kind of model implies that growth would proceed linearly from a relatively minute portion of the cell. The kinetics of cell growth follow an autocatalytic law and so are not consistent with this thesis. He therefore suggested that perhaps "duplicates or partial duplicates of genes reach the cytoplasm when the nuclear membrane disappears in mitosis and that these can produce duplicates in turn, and so on, permitting exponential increase." To explain the fact that cytoplasmic inheritance is rarely observed he assumes that the self-duplicating capacity of these free genic replicas is subject to decay. Those that retain this capacity indefinitely he called "plasmagenes."

Again, in connection with cellular differentiation Wright (*22*) points out that the heritable stability of the differentiated state is more easily understood if we assume the existence of self-duplicating cytoplasmic components (plasmagenes) which can undergo controlled mutations. Stimulated by the fundamental observations of Sonneborn (*13*), Darlington (*4*) also postulated the existence of a cytoplasmic self-duplicating unit which he called the "plasmagene" and which he assumed controls heredity at the "molecular level."

References

1. Avery, O. T., McLeod, C. M., and McCarty, M. J. *J. exp. Med.*, 1944, **79**, 137.
2. Caspersson, T., and Brandt, K. *Protoplasma*, 1940, 35, 507.
3. Cori, C. F. *Biol. Symposia*, 1941, **5**, 131.
4. Darlington, C. D. *Nature, Lond.*, 1944, **154**, 164.
5. Greenstein, J. *Adv. prot. Chem.*, 1944, **1**, 209.
6. Lindegren, C. C. *Bact. Rev.*, 1946, **9**, 111.
7. Lipmann, F. *Adv. Enzymol.*, 1941, **1**, 99.
8. Martin, A. W., and Field, J. *Proc. Soc. exp. Biol. Med.*, 1934, **32**, 54.
9. Moog, F., and Spiegelman, S. *Proc. Soc. exp. Biol. Med.*, 1942, **49**, 392.
10. Pontecorvo, G. *Nature, Lond.*, 1946, **157**, 95.
11. Potter, V. R. *Science*, 1945, **101**, 609.
12. Schultz, J. *Symp. quant. Biol.*, 1941, **9**, 55.
13. Sonneborn, T. M. *Proc. nat. Acad. Sci.*, 1943, **29**, 329.
14. Spiegelman, S. *Ann. Mo. bot. Garden*, 1945, **32**, 139.
15. Spiegelman, S., Kamen, M. D., and Dunn, R. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, **5**, 99–100.
16. Spiegelman S., Lindegren, C. C., and Lindegren, G. *Proc. nat. Acad. Sci., Wash.*, 1945, **31**, 95.
17. Thomas, P. T. *Nature, Lond.*, 1945, **156**, 172.
18. Winzler, R. J., Burk, D., and du Vigneaud, V. *Arch. Biochem.*, 1944, **5**, 25.
19. Woods, M. W., and DuBuy, H. G. *Phytopathology*, 1943, **33**, 766.
20. Woods, M. W., and DuBuy, H. G. *Science*, 1945, **102**, 591.
21. Wright, S. *Physiol. Rev.*, 1941, **21**, 487–527.
22. Wright, S. *Amer. Nat.*, 1945, **79**, 289.

Obituary

Enoch Karrer

1887-1946

The field of textile research lost a valuable physicist in the death of Enoch Karrer on 27 March 1946 at Marine Hospital, New Orleans, Louisiana, following a short illness. Dr. Karrer was in charge of the Physics Section, Cotton Fiber Research Division, Southern Regional Research Laboratory.

Dr. Karrer came in 1936 to the Cotton Division, Bureau of Agricultural Economics, U. S. Department of Agriculture, in which the cotton investigations were then being conducted. The investigation of the physical properties of cotton fibers was a relatively new field to Dr. Karrer, who had given many of his earlier years to problems connected with light, optics, physiological stimulus of animals, rheology of rubber, and the like. This work was subsequently moved to the New Orleans laboratory.

Enoch Karrer was born at Rich Hill, Missouri, on 23 May 1887. After completion of grade and high school at Ellensburg, Washington, he attended the state university at Seattle, where he received the A.B. and M.A. degrees in 1911 and 1912, respectively. During 1913 and 1914 he was a fellow at Johns Hopkins University and was awarded the Ph.D. degree at the end of the latter year.

For several years following the completion of his formal education Dr. Karrer was associated with the United Gas Improvement Company, Philadelphia,

Pennsylvania. In this capacity he worked on such problems as methods for determination of the radiant luminous efficiency of light sources, factors affecting the relation of photoelectric current and illumination, construction of vacuum gauges, and the efficiency of light from the electric arc and from microorganisms. In 1919 the Franklin Institute awarded Dr. Karrer, jointly with Herbert E. Ives and E. F. Kingsbury, the Edward Longstreth medal of merit for outstanding optical research.

For about a year during World War I he served the Government in Washington in the capacity of research engineer, and in 1918 he joined the National Bureau of Standards as associate physicist in the Searchlight Section, of which he later became chief. Here he extended his work on light, covering contrast sensitivity of the eye, relative spectral transmission of the atmosphere, and more accurate methods for measurement of light intensity.

During 1921 Dr. Karrer left the Bureau to become physicist of the National Lamp Works of the General Electric Company at Nela Park, Cleveland, Ohio. Papers, some of which were published in German journals, continued to appear in the field of applied research on the improvement of apparatus, the properties of different lamps, and the biological effects of light.

In 1923, in addition to his activities at the Nela Park Laboratory, Dr. Karrer became research associate at the Cushing Laboratory for Experimental Medicine, Western Reserve University. Here, in association with H. C. Stevens, one of his former teachers at Washington State University, he conducted researches extending over 12 years and culminating in some nine papers in the field of muscle activity and medical instrumentation. Undoubtedly Dr. Karrer's great interest in medical phenomena throughout the remainder of his life stemmed from this long association.

In 1926 Dr. Karrer transferred from the Lamp Works to the Cleveland Wire Works of the General Electric Company, and later in the same year to the B. F. Goodrich Company, Akron, Ohio, where he undertook measurements of the plasticity of rubber and developed a new instrument for this purpose. One especially interesting title for this period reads: "A method of blood transfusion by means of rubber tubes vulcanized on the blood vessels." During this period also, a number of patents were issued to him and assigned to the B. F. Goodrich Company. In 1932 he left the Company and for approximately three years gave his full time to Western Reserve University.

Dr. Karrer was an author of approximately 70 publications in the scientific field in addition to some half-dozen patents. At the time of his death he had many phases of investigation in various stages of development, and the stage seemed to be set for his former fruitful flow of papers.

In his attitude toward research Dr. Karrer was fundamental and extremely antagonistic toward halfway measures and expedients, and had a profound sense of ethics in the scientific field. His ingenuity and experience as well as his kindly smile will be greatly missed among his many colleagues and friends.

CARL M. CONRAD

New Orleans, Louisiana

Philippe Lasseur

1882-1946

Philippe Lasseur, professor of microbiology in the Faculté de Pharmacie, Université de Nancy, France, died on 10 January 1946 from complications following an attack of pneumonia. He was 63 years of age.

Prof. Lasseur, who served in the French Army during World War I and was made a chevalier of the Legion of Honor in 1934, was the author or joint author of over 200 papers on microbiology. His work in this field covered a wide range, but he is perhaps best known for his studies on the conditions affecting growth and pigment production by dissociated types of various species of chromogenic bacteria. In 1928 he founded the annual publication, *Travaux du laboratoire de microbiologie de la faculté de pharmacie de Nancy,* in which most of his later work was published. Despite the difficulties of World War II, he was able to continue his work as well as the publication of this journal, of which Fascicule 14 appeared in 1945.

His death marks the end of an era, but it is to be hoped that his students will be able to continue the work which he carried on for so many years.

WALTER C. TOBIE

Old Greenwich, Connecticut

Bernice Maclean Shapiro

1903-1946

Bernice Maclean Shapiro, assistant professor of biology at Hunter College and former chairman of that Department, died on 8 March 1946. She was born on 20 November 1903 in Waterbury, Connecticut, of Scottish ancestry reaching back to Duart Castle on the Isle of Mull.

At Mount Holyoke College, from which she was graduated with high honor in 1926, she majored in zoology and was elected to Phi Beta Kappa.

During the next year she served as an assistant in zoology at Mount Holyoke and the year following was appointed instructor. During her instructorship, from

1927 to 1929, she became increasingly interested in zoology and thoroughly demonstrated her scholarship, enthusiasm, and teaching ability. Her paper on hermaphroditism in the frog shows the thoroughness of her work in this period.

In 1929 she was awarded the Mary E. Woolley Fellowship by Mount Holyoke College and went to Columbia University, where she began work in experimental embryology in the Department of Anatomy. In her second year at Columbia she was awarded a graduate fellowship from that university and also was appointed instructor. In this capacity she continued her own investigations and gave laboratory instruction in medical histology from 1929 through the summer session of 1931. A part of the next year was devoted to an investigation in the Department of Ophthalmology the results of which were included in papers on the embryology of Amblystoma, published with H. B. Adelmann. She received her doctorate from Columbia University in 1933. Her published papers from that study, some of them with S. R. Detwiler, are concerned with the growth of engrafted embryonic spinal cord of Amblystoma.

In the autumn of 1933 Dr. Shapiro began work in the Department of Biological Sciences at Hunter College, becoming assistant professor in 1937 and serving as chairman of the Department from 1941 to 1944. Although heavy administrative duties were added to her teaching, which included courses in embryology, comparative anatomy, and general zoology, she found time to continue research with her husband, Harry L. Shapiro, on the development of the tooth germs in the mammal.

Up to the time of her death she continued to plan for further study and for her return to her students at Hunter College.

ANN H. MORGAN
Mount Holyoke College, South Hadley, Massachusetts

Technical Papers

A Possible Avian Analogue of the Scrotum

R. B. COWLES and A. NORDSTROM
Department of Zoology, University of California, Los Angeles

The phenomenon of heat-induced sterility is a familiar one and long has been noted as a characteristic of all species of mammals that have been studied from this viewpoint (*1*). Similarly, in insects where this trait has been sought its presence has been demonstrated, as in *Drosophila* and *Ephestia*. Indirect and some direct evidence has suggested the presence of heat-induced sterility in the remaining major groups of terrestrial animals.

Because nothing was known regarding the possible existence of this phenomenon in reptiles, these animals were tested in our laboratories for the trait, and it was clearly demonstrated in the first species studied, *Xantusia vigilis* (*2*). Because reptiles were a key group in the origin and evolution of birds and mammals, the presence of this character, even in the highly specialized modern forms, is of considerable interest.

With regard to birds, Riley (*3*) has reported that spermatogenesis in the English sparrow takes place intermittently and that the time of greatest spermatogenic activity is confined to the last hours of the night, when the body temperature is at its lowest level. This is consonant with the theory of heat sensitivity of the germ cells and suggests the need for more extended studies on the thermo-spermatogenic relationships in birds.

Because of the apparently universal occurrence of a heat-induced sterility resulting from the dual standard of heat tolerance, it has been proposed (*1*) that the phenomenon may have played a dominant part in the evolution of most or possibly all terrestrial animals, and that thus it was logical to suggest the possibility that, whatever other factors might have been involved, the predominant influence in archosaurian extinction might have been the result of overheating. If this can be substantiated by future studies of paleoclimates, this dramatic event may provide us with additional and important support for the proposal that this dual thermal capacity has extended to archaic animals and is not a new feature.

Because birds retain many characteristics that are reptilian and because they operate at the highest temperatures known among the vertebrates, yet have internally located testes, they have posed a serious question which was only partially answered by Riley's studies.

Attempts to measure the presumable existence of a temperature differential between the testes and the rest of the body so far have failed. In view of Riley's findings, this lower temperature in the region of the testes is not a necessary condition for normal spermatogenesis, but its presence would be a logical

expectation. Up to the present we have ascribed this failure to demonstrate a lower testicular temperature to inadequacies in technique, but it is possible, though improbable, that no such differential exists. The improbability is based on the almost invariable thermal gradient between the hot-bodied bird and the cooler environment. Thus, if tropical species of birds have temperatures approximating those of their temperate-zone relatives, the favorable nature of the gradient would be 42–43° C. in the birds (often still higher when they are active) to 29–30° C., the mean annual air temperature.

Because of the failure in the physiological investigations it seemed advisable to re-examine the location of one of the morphological characteristics that might be credited with the hypothetical lowering of the testicular temperature, namely, the air sac system.

In order to obtain an accurate picture of the natural relationships of the visceral organs, the birds were not inverted to the usual position employed in anatomical studies or while being "sexed" during the preparation of scientific skins. Omission of this technique may have been the factor that has obscured the true relationships of testes to air sacs. While in their normal position the air sac systems of the birds used (*Euphagus cyanocephalus,* Brewer's blackbird) were injected with a latex solution.

These studies were continued over two successive seasons of the testicular cycle, and they clearly demonstrated that the testes move a short but important distance downward and backward, so that during the warm spring months while spermatogenesis is in progress *the testes become enveloped between the two dorsal folds of the abdominal air sacs.*

In this as in all other species of Nearctic birds a late spring or summer testicular regression takes place, and the behavior of the organs strongly suggests that the insulating or cooling propensities of the air sacs are not fully adequate to prevent some heat damage, but a sufficient measure of relief is accorded the birds to enable them to reproduce before collapse of gonads takes place.

The entire performance so closely resembles the picture of heat-induced collapse in other animals that it has been deemed advisable to continue similar studies in order to determine whether this similarity is superficial, a result of light changes, or mere coincidence, or whether it is genuine heat effect. It is believed that prolonged but moderate overheating will prove to be a major factor.

References

1. Cowles, R. B. *Amer. Nat.*, 1945, **79**, 160–175.
2. Cowles, R. B., and Burleson, G. L. *Amer. Nat.*, 1945, **79**, 417–435.
3. Riley, G. M. *Soc. Biol. Med.*, 1937, **34**, 331.

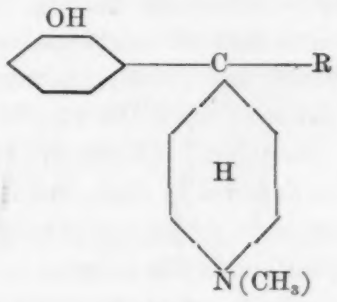
Comparison of Some New Analgesic Compounds

Charles C. Scott, E. B. Robbins, and K. K. Chen[1]

Lilly Research Laboratories

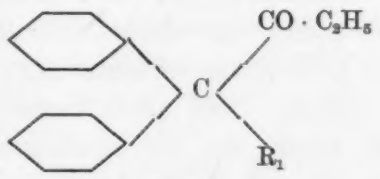
Eli Lilly and Company, Indianapolis, Indiana

Knowledge of new analgesic agents prepared by German chemists has recently been published by the U. S. Department of Commerce (*4*). A number of these substances possess marked pharmacologic properties. A report on one outstanding member of this group has already been made from this laboratory (*5*). It is, chemically, 1,1-diphenyl-1-(dimethylamino-isopropyl)butanone-2 (German Serial No. 10820). However, other compounds in the series appear to have good possibilities and deserve further study, particularly from a clinical point of view. The following is a brief comparison of six of the compounds with demerol and 10820. As shown by the following structures, three of them are closely related to 10820, and the other three, to demerol. In fact, demerol is identical with 10446 except that it has no OH-group in



(I)

R = $COO \cdot C_2H_5$ [10446]
= $CO \cdot C_2H_5$ [10720]
= $CO \cdot CH_3$ [10726]



(II)

$R_1 = CH_2 \cdot CH(CH_3) \cdot N(CH_3)_2$ [10820]
$= CH_2 \cdot CH_2 \cdot N(CH_3)_2$ [10582]
$= CH_2 \cdot CH_2 \cdot N$ (H) O [10581]
$= CH_2 \cdot CH(CH_3) \cdot N$ (H) [10819]

the metaposition of the benzene ring. The substances other than demerol, designated by their original German numbers, were prepared by Drs. T. P. Carney and E. Rohrmann, of our organic chemical department.

Methods. Analgesic action was determined in rats

[1] Thanks are due Francis W. Israel for technical assistance in this study.

by the method of Haffner (*2*) and in dogs and man by thermal radiation technique (*1, 3*). In rats and dogs the substances were administered by intraperitoneal injection, and in man, by mouth. Effects on circulation, respiration, and salivary (submaxillary) flow were measured with standard procedures in dogs under barbiturate anesthesia. In this case, injections were all made intravenously. The median lethal dose in mice by intravenous injection was ascertained for each compound.

TABLE 1

COMPARISON OF THE PHARMACOLOGIC ACTION OF A SERIES OF NEW ANALGESIC AGENTS

Compound No.	$LD_{50} \pm$ S. E. in mice by vein (mg./kg.)	Analgesic action: threshold dose			Action in anesthetized dog by vein				
		Rat (mg./kg.)	Dog (mg./kg.)	Man (mg.)	Dose (mg./kg.)	Blood pressure (mm. Hg)	Heart rate	Respiration (%)	Depression of saliva
Demerol	40.8 ± 1.4	8	10	100–150	1	− 65	Unchanged	+ 110	Marked
10446	85.3 ± 5.8	5	10	80	5	− 60	"	+ 33	"
10720	13.7 ± 1.0	1	2	7.5	1	− 70	Slowed	− 53	Moderate
10726	104.0 ± 5.8	8–16	16		10	Unchanged	Unchanged	Unchanged	Slight
10820	17.3 ± 0.9	1	1	5	2	− 25	Slowed	− 56	"
10582	31.4 ± 2.4	2	4–8	20–30	2	− 40	"	− 33	"
10819	17.8 ± 1.3	2	2	5	1	− 30	"	− 28	"
10581	29.4 ± 2.0	2			1	− 20	"	− 42	"

Results. Table 1 shows the findings for the various tests. It is obvious that six compounds (10820, 10446, 10582, 10581, 10819, and 10720) are more active analgesically than demerol when the results in rats, dogs, and man are compared. Compound 10446 has the same potency as demerol in dogs, but it is more effective in rats and man. The introduction of an OH-group at metaposition in the benzene nucleus (10446) increases the analgesic action of demerol. The ketone form (10720) is more potent than the ester form (10446). Compound 10726 caused such severe vomiting that it was not tested in man. All the diphenyl derivatives are ketones and have a relatively high potency. No study was made with 10581 in dogs and man due to shortage of material.

Analgesic potency and acute toxicity appear to parallel each other, but the relationship is by no means exact. The effects on blood pressure of anesthetized dogs show marked differences. Considerable and prolonged fall of blood pressure followed injection of the demerol derivatives, with one exception (10726). The depressor effects of the diphenyl compounds were less marked.

Cardioinhibition resulted from administration of any of the diphenyl substances, but only one of the demerol group (10720) produced this effect. Cardiac slowing was apparently due to stimulation of the vagal center, since it could be abolished by section of the vagus nerves or atropinization.

Striking differences were observed in the effects on respiration. Stimulation resulted from administration of the esters, whereas depression occurred with the ketones. Whether or not this is a coincidence will depend on further work with more compounds of the same series.

Inhibition of salivary secretion approaching that caused by atropine was noted with the esters. The ketones, however, showed much less effect.

Four new compounds were tested on man along with demerol and 10820. With threshold doses, certain mild side reactions were encountered with all of them. The most frequent symptom was lightheadedness (not true vertigo), the intensity of which appeared to vary with the degree of analgesia. Nausea and vomiting were relatively rare in the doses studied.

References

1. ANDREWS, H. L., and WORKMAN, W. *J. Pharm. exp. Therap.*, 1941, **73**, 99.
2. HAFFNER, F. *Dtsch. med. Wschr.*, 1929, **55**, 741.
3. HARDY, J. D., WOLFF, H. G., and GOODELL, H. *J. clin. Invest.*, 1940, **19**, 649.
4. KLEIDERER, E. C., RICE, J. B., CONQUEST, V., and WILLIAMS, J. H. Report No. 981, Office of the Publication Board, Department of Commerce, Washington, D. C.
5. SCOTT, C. C., and CHEN, K. K. *Fed. Proc.*, 1946, **5**, 201; *J. Pharm. exp. Therap.*, 1946, **87**, 63.

Scanning Science—

The Commissioner of Labor has submitted to the House of Representatives a plan for the organization of a permanent Census Bureau in Washington. The Director of the Census will be paid $6000 a year, the Assistant Director $4000. In addition there are to be three clerks and five statisticians. It is provided that a general census shall be taken April 15, 1900, and every ten years thereafter.

—18 December 1896

Science Exhibition

The Science Library
Booth Nos. 15–22

The Science Library, an annual cooperative exhibit by leading book publishers, this year has more than fifty sponsors. Nearly eight hundred new and standard science textbooks and established reference works have been nominated for display. A list of the books on exhibit with complete title, authors, publisher, and price will be available for visitors to the booth. This list will be combined later to form the basis of an *Occasional Publication of the AAAS* with the subtitle "Scientific and Technical Books of 1946." Both of these publications will be available to members gratis as long as the supply lasts. It is expected that the complete list will be ready in February, 1946. Through the cooperation of The Technical Library Consultants of New York several new features have been added in the exhibit. Mr. W. Phillip Leidy and Mr. Kenneth Shahabian will be in attendance at the booth to explain and demonstrate new developments in library science that may be used advantageously by scientists.

Meteorological Instrumentation
Army Air Forces and Signal Corps
War Department

The Army Air Forces and the Signal Corps are collaborating in this exhibition, presenting advancements in the fields of synoptic meteorology and meteorological instrumentation. The Air Weather Service, an arm of the Army Air Forces, is responsible for supplying current weather information and forecasts as required by the Army; the Signal Corps is responsible for the development of new meteorological instruments and equipment and for furnishing all meteorological material to the U. S. Army. In this exhibit, the displays of the various charts employed in weather station operation are provided by the Air Weather Service. These charts include synoptic weather maps illustrating methods of surface and upper atmosphere analysis. The displays of equipment and instruments used in obtaining meteorological information are provided by the Signal Corps. Limitations of space have necessitated restricting the number of pieces of equipment displayed; in some instances, particularly where bulky items cannot be accommodated, photographs are employed to illustrate, as far as possible, the recent advances made in experimental meteorology. The exhibit consists of: (1) *Sferics*—A method for locating the source regions of lightning discharges by using radio direction finding techniques, (2) *Weather Radar*—Radar instrumentation used for studies of precipitation areas, (3) *Radiosondes*—Instruments for the measurement of temperature, pressure and relative humidity in the troposphere and lower stratosphere, (4) *Aircraft Weather Equipment*—Instruments for measuring temperature and moisture content from a plane in flight, and (5) *Automatic Weather Station*—Clock controlled weather station which measures temperature, pressure, relative humidity, wind direction and speed, cumulative rainfall and relative sunshine. Values of the various elements are transmitted from the remote stations to a centrally located radio receiving station.

Office of Naval Research
U. S. Navy
Washington, D. C.

Scientific personnel will be featured in an exhibit prepared by the Office of Naval Research. The exhibit centers around a map of the U. S. showing locations of Naval research and development laboratories. The special fields of science, scientific personnel engaged, and salary ranges for professional positions will be displayed. Representatives of the Scientific Personnel Branch of the Office of Naval Research will be at the exhibit to discuss opportunities for scientists in the Navy's research and development program.

U. S. Coast and Geodetic Survey
Department of Commerce
Washington, D. C.

The display of the Coast and Geodetic Survey will feature the results of recent research on special forms of maps designed to show topographical relief features of both land and ocean bottoms. The entire process for manufacturing the maps was developed by members of the Survey staff.

The Technicon Company
New York, N. Y.
Booth Nos. 14–15

(1) The AUTOTECHNICON, a machine for the automatic processing of tissues. The Autotechnicon fixes tissues (by any method) washes, dehydrates, clears, infiltrates and stains, ready for mounting. Operating independent of human intervention, it will process daily surgical tissues overnight, ready for microscopy in the morning, permitting speedy diagnosis, offering impressive economies in time and labor; (2) The SCOPICON, a mobile high-powered projector for microslides and color transparencies. Employs either microscope or built-in low-power magnification stages. New pressure-mercury-arc system provides ultra-intense light sources for brilliant flickerless projection, either on wall-screen (for large-group viewing) or within auxiliary table-mounted dark chamber (for small group study). Attachments for photomicrography, monotone or full-color; (3) The Labaid all-steel laboratory filing cabinets. Interchangeable drawers to file microslides (flat or vertically), transparencies, lantern slides, index cards, *all in the same unit*; (4) The Technicon automatic PIPETTE WASHER is a heavy-duty device for large-volume pipette washing. Pipettes require no repeated handling: a full load is gathered, washed, dried in the same basket. Unique automatic washing principle delivers sparkling-clean pipettes in three-minute washing period.

News and Notes

The Atomic Energy Commission announced on 11 December that it would assume formal control of the Manhattan Engineer District soon after 1 January. Since the Commission was appointed on 28 October (See *Science* 8 November and 13 December) it has had a series of conferences with members of the War Department preparatory to taking active control of a plant valued at $1,400,000,000 with approximately 43,000 employees.

To aid the Commission President Truman appointed a nine-man General Advisory Committee specifically authorized to consult with the Commission on "scientific and technical matters relating to materials, production and research, and development" on 12 December. The new Committee is made up of James B. Conant, president of Harvard; Lee A. DuBridge, president, California Institute of Technology; Enrico Fermi, professor of physics, University of Chicago; I. I. Rabi, professor of physics, Columbia University; J. R. Oppenheimer, formerly director of the Los Alamos Laboratories of the Manhattan Project, and now professor of theoretical physics, University of California; Glenn T. Seaborg, professor of chemistry, University of California; C. S. Smith, director of the Institute of Metals, University of Chicago; Hartlev Rowe, vice-president and chief engineer of The United Fruit Company; and Hood Worthington, chemical engineer, E. I. du Pont de Nemours & Co.

About People

Harlow Shapley, director of the Harvard College Observatory, left on 27 November for Mexico City, where he attended the inauguration ceremonies for President-elect Licenciado Miguel Aleman, as the President's personal guest. Dr. Shapley, who represented American science at the inauguration, will also take part at a meeting of the Latin-American Club of the Scientific Research Society of America, of which he is national president.

Staff members of the Harvard Observatory under Dr. Shapley's direction have, during the past few years, aided in the creation of the National Astrophysical Observatory in Tonanzintla, Puebla, and in the operation of the Comite Interamericano de Publicationes Cientificas, which has taken the lead in building up Mexico's scientific libraries. In addition, Dr. Shapley has also planned and conducted two scientific congresses in Mexico, one dealing with astronomy and one with physics.

While in Mexico City, Dr. Shapley also plans to discuss the possibilities with Mexican publishers of translating American scientific books into Spanish.

Previous recognition of Dr. Shapley's work in Mexico has brought him the Cross of Honor from Puebla, an honorary degree from Michoacan, membership in the Mexican National Academy of Sciences, and the Aztec Eagle.

Brig. Gen. Raymond A. Kelser, director of the Veterinary Division of the Surgeon General's Office, U. S. Army, during the war, was awarded the Gorgas Medal at the annual convention of the Association of Military Surgeons in Detroit on 9 October. The medal is awarded under the auspices of Wyeth, Inc., of Philadelphia, and is given annually by the Association for outstanding work in preventive medicine for the armed forces. Gen. Kelser's work was that of eradicating rinderpest, a cattle disease, in the Philippine Islands, making it possible for the Filipinos to develop a domestic milk supply. Dr. Kelser is now retired from active service and is dean of the College of Veterinary Medicine and professor of bacteriology at the University of Pennsylvania.

H. Jermain Creighton, Swarthmore College, received the Edward Goodrich Acheson Gold Medal and $1,000 prize at the Electrochemists' Congress held in Toronto, Canada, on 16–19 October. In his acceptance speech, Dr. Creighton revealed a number of inventions and discoveries made in electrochemistry during the war.

R. M. Strong has retired, after 28 years as professor and head of the Department of Anatomy, Loyola University School of Medicine, with the title of chairman and professor emeritus, and has been appointed research associate in anatomy at the Chicago Natural History Museum (Field Museum).

Raymond L. Taylor, formerly associate professor of biology, College of William and Mary, has been appointed resident head of biology at Sampson College, one of the recently organized Associated Colleges of Upper New York (see *Science,* 1946, **104**, 366).

Ralph A. Galbraith was appointed professor of electrical engineering and chairman of the Department, Syracuse University, on 1 September, succeeding Charles W. Henderson, who has relinquished the chairmanship because of ill health.

Nancy Graham Rogers received the first Exceptional Civil Service Award given by the Army to a woman, at Walter Reed Hospital, Washington, D. C., on 30 October. Miss Rogers received the award for her services as bacteriologist with the Division of Virus

and Rickettsial Diseases, Army Medical Center. The citation referred to her important work in developing vaccines while on a mission to Guatemala in 1943.

William K. Carpenter, Wilmington, Delaware, returned on 17 November by air from Africa, where he had been since June collecting specimens for two habitat groups in the museum of the Academy of Natural Sciences, Philadelphia. Mr. Carpenter is the son of R. R. M. Carpenter, a trustee of the Academy, who in recent years collected the specimens and installed a number of life groups in North America and African Halls. According to present plans, the recent African expedition will result in a new marsh group and a habitat group of wild dogs.

Conrad E. Ronneberg, formerly chairman of the Division of Physical Sciences, Herzl Branch, Chicago City College, is now professor and chairman, Department of Chemistry, Denison University, Granville, Ohio. He was awarded the Bronze Star Medal for his service as Commandant, Army Information and Education Staff School, European Theater of Operations, where he served as a lieutenant colonel.

William A. Lewis, Jr., research professor of electrical engineering at Illinois Institute of Technology, became dean of the Institute's Graduate School on 1 September, succeeding Linton E. Grinter, dean since 1937, who resigned to devote his time to teaching and research.

Lyman C. Duryea has been made medical director of the Research Council on Problems of Alcohol, according to Anton J. Carlson, president of the Council. Dr. Duryea was formerly medical director of the Veterans Administration in New York State. Joseph Hirsh, formerly director of Medical Administration of the Veterans Administration for hospitals and clinics in New York State, is associate director in charge of education and public relations.

A. C. Ivy, vice-president of the University of Illinois, has been awarded a special gold medal by the American Roentgen Ray Society for research achievements.

Milton O. Lee, recently released from the Army, has rejoined the staff of the Memorial Foundation for Neuro-Endocrine Research, Harvard Medical School. He will be on duty at Worcester State Hospital, Worcester, Massachusetts.

Marshall Hall, formerly of Yale University, and Howard H. Alden, University of Wyoming, have joined the staff of the Mathematics Department, The Ohio State University.

W. L. Waterhouse, reader in the Faculty of Agriculture of the University of Sydney, Australia, was appointed by the University Senate at its last meeting to be research professor in agriculture in recognition of his work in cereal pathology.

Chauncey D. Leake, vice-president of the University of Texas Medical Branch, Galveston, was the principal speaker at a meeting of the Riverside County Medical Society of Southern California in Palm Springs on 9 November. The meeting was held to commemorate the anniversary of anesthesia. Among the guests was John Parkinson, cardiologist of London.

George F. Hanson has been appointed instructor in geology at Union College, Schenectady.

Edward C. Reifenstein, Jr., formerly Harvard Medical School research fellow at the Massachusetts General Hospital, Boston, has been appointed research consultant to the Sloan-Kettering Institute for Cancer Research at the Memorial Hospital Cancer Center, New York City. He has also been named as clinical research consultant to Ayerst, McKenna & Harrison, Ltd., New York City. At Boston, Dr. Reifenstein assisted Fuller Albright in investigations on endocrine and metabolic disorders; at the Sloan-Kettering Institute, he will carry on clinical research on the relation of glandular disturbances to cancer. He will continue as secretary and editor of the *Transactions* of the Conferences on the Metabolic Aspects of Convalescence, which are being held two or three times a year under the auspices of the Josiah Macy, Jr. Foundation.

Arthur Lejwa was recently appointed scientific director of the Robert Gould Research Foundation and its Institute for Nutritional Research, Erlanger, Kentucky.

Raymond J. Seeger, secretary of Section L of the AAAS, received the distinguished service award, highest Navy award for civilians, on 22 November at special ceremonies. Dr. Seeger was cited for outstanding work as physicist in the Research and Development Division of the Bureau of Ordnance during the war. His signal achievement was described as "comprehensive investigation on the reflection of shock waves in air and in rigid surfaces. The result of an extensive exploratory program initiated by Dr. Seeger on the basis of this investigation corroborated its major discoveries, culminating in the so-called 'Mach' effect. The basis of the air-burst principle found its ultimate use in the bomb explosion over Japan." Dr. Seeger was research consultant in theoretical physics at the Bureau of Ordnance from September 1942 to November 1946. Last month he was named chief physicist in charge of the Mechanics Division, Research Department, Naval Ordnance Laboratory, White Oaks, Maryland.

Thomas H. King and *Richard H. Bohning* have been appointed assistant professor and extension plant pathologist, and assistant instructor in botany, respectively, at The Ohio State University.

Babette I. Brown, formerly at Cornell University, has been made instructor in botany at the University of Rochester, New York.

Robert D. Potter, for the last six years Science Editor of the *American Weekly,* announces that he is resigning from that publication 1 January to found a private organization to be known as The Wordshop, Scarborough, New York. The purpose of the new organization is to report and interpret science and technology to the lay public through mass media, including the radio. Mr. Potter was formerly staff physics writer for Science Service, and was at one time Science Editor of the *New York Herald Tribune.* He is one of the founders of the National Association of Science Writers and has twice served as its president.

Stephen S. Kane has been appointed assistant professor of chemistry at the New Jersey City Junior College, Jersey City. Prior to his war service in the Navy, he was chemist for the Apex Smelting Company, Chicago.

Lt. Col. Frank L. Hawkins, Chemical Warfare Service, has recently returned from a military government assignment in connection with the German chemical industry and has been released by the Army. He has returned to his civilian duties at Edgewood Arsenal, Maryland, and has been appointed assistant chief, Design Branch, Plants Division, CWS Technical Command.

W. E. Clapper, assistant professor of bacteriology, University of Utah School of Medicine, has resigned to accept a similar position at the University of Colorado School of Medicine.

Edward L. Ullman, formerly director, Joint Intelligence Study Publishing Board, The Joint Chiefs of Staff, has jointed the staffs of geography and regional planning at Harvard University as assistant professor.

Donald C. Gregg, Amherst College, has been made assistant professor of chemistry at the University of Vermont. During the past summer he was visiting lecturer in chemistry at Harvard University.

Robert L. Pendleton, of the Office of Foreign Agricultural Relations, U. S. Department of Agriculture, has been appointed professor of tropical agriculture and soils, Department of Geography, The Johns Hopkins University. He will spend the fall semester in this post and the rest of the time with OFAR.

George E. Mueller has been appointed assistant professor of electrical engineering at The Ohio State University.

Thorold Vogt, of Trondheim University, Norway, has written to Charles H. Behre, Jr., of Columbia University, that he was one of three in a group of 20 that did not suffer seriously at the hands of the enemy during the occupation of his country. He also wrote that "Carl Bugge, director of the Geological Survey of Norway in Oslo, got safely through the war. Important maps and papers belonging to the Survey which it was not desirable that the Germans should get hold of and which it was important to preserve he succeeded in placing in a mine at Kongsberg Solvverk. The offices of the Geological Survey at Oslo were badly damaged during the bombing on 25 September 1942, but all collections, archives, and the library were saved."

Visitors From Abroad

C. B. Fawcett, University College, London, and Mrs. Fawcett left Southampton aboard the *Washington* on 12 December to attend the AAAS Boston meeting, at which Prof. Fawcett will represent the British Association for the Advancement of Science. Prof. Fawcett will deliver an address on 30 December on "The Numbers and Distribution of Mankind." As previously reported in *Science,* Prof. Fawcett will be available for engagements from 1 January until he assumes his duties as visiting professor at Clark University Graduate School of Geography on 1 February.

Paul Larsen, plant physiologist from the University of Copenhagen, has arrived here on a Danish-American Society fellowship to do research in plant hormones in the Mathies Botanical Laboratory at Connecticut College.

Meetings

The Optical Society of America will hold its winter meeting at the Hotel Pennsylvania in New York City on 20–22 February 1947. Despite numerous invitations from other parts of the country, the Board of Directors again selected New York in conformity with the traditional peace-time schedule of a winter meeting in that city and an October meeting elsewhere. The Program Committee is arranging a number of special features that will be listed in the final announcement, to be made later this month. Those who intend to contribute papers are urged to submit their abstracts as promptly as possible in order that the Program Committee may be able to gauge the interests of the members and to organize sessions on special topics. In case a member hopes to present a paper for the winter meeting but is unable to submit an abstract as this time, a letter indicating the probable title will be of assistance.

Announcements

More than 2,000,000 students, a 50 per cent increase over the previous peak enrollment, are now attending the 1,749 colleges and universities of the United States, it was reported on 19 November by Francis G. Cornell, chief of the Research and Statistical Service of the U. S. Office of Education, Federal Security Agency.

The total of 2,062,000, based on a 15 October survey by the Office of Education, was compared with the previous October peak enrollment of 1,360,000 reported in the prewar year 1939–40. The 1946 Office of Education survey covered those students attending classes or lectures conducted by the regular colleges and schools but did not include students enrolled in extension or correspondence courses.

John Dale Russell, director of the Higher Education Division of the Office of Education, in commenting on the record enrollment, stated: "The present student load, which is more than double the 950,000 total of last year, has heavily taxed the resources of almost all higher educational institutions in providing adequate staff, housing, and classroom facilities. Every effort has been turned to supplying the demand for admission to college, particularly on behalf of veterans entitled to educational benefits under Public Laws 346 and 16."

In 1945 there were fewer than 50,000 veterans enrolled in higher educational institutions. This year there are 1,073,000 veterans enrolled, or approximately one-half of the present total number of students. Almost half of all students and more than half of the veterans are enrolled in the 131 larger institutions.

According to the survey, more women (667,000) are attending college this year than ever before, even though the percentage of the total has dropped markedly, due largely to the phenomenal increase of men veterans. This year, men students constitute 32 per cent of the total, as contrasted with 61 per cent in 1945, 63 per cent in 1943, and 39 per cent in 1941.

The Office of Education information was based upon a preliminary report of a sample survey of higher educational institutions made as of 15 October.

The Office of Education is now communicating with selected educational officials throughout the country to determine the extent to which the expansion of college facilities has been sufficient to accommodate all qualified persons, veterans and nonveterans, seeking admission to college this year.

Important advances in knowledge of nutrition and its relation to life and health have been made through scientific research supported by grants of the Nutrition Foundation, George A. Sloan, president of the Foundation, stated at a luncheon meeting following the fifth annual meeting of the Board of Trustees in New York on 14 November. "This Foundation," Mr. Sloan said, "has had a part in alleviating suffering caused by diabetes, anemia, and tooth decay. The work it has supported has brought advances in knowledge of the relation of nutrition to maternal and infant health, bone healing, and liver injuries. It has helped to increase the useful life span." The Nutrition Foundation, Mr. Sloan reported, has made a total of 133 grants, aggregating $1,267,305 to 53 universities and medical centers in the United States and Canada. The work of the Foundation has been supported by contributions, totaling $2,318,000, made by food and related manufacturers.

The Board of Trustees has approved renewals of grants amounting to $29,050 and new grants totaling $28,800. The latter were made to: Olaf Bergeim, University of Illinois, to study 10 or more individual amino acids in human and animal blood, tissues, sweat, and spinal fluid, in health and disease ($3,000); Paul D. Boyer, University of Minnesota, to study the mechanism of the action of vitamin E and especially the relationship between deficiencies and impaired functions of the muscles ($2,600); Ralph I. Dorfman and J. T. Wearn, Western Reserve University, to study the nature of relationships between vitamins and hormones ($3,400 each); Carl M. Lyman, A. and M. College of Texas, to study the steps by which amino acids are synthesized by living organisms ($2,000 annually for two years); Joseph H. Roe, George Washington University, to study methods for making an analytical distinction between two or possibly more of the oxidation products of vitamin C ($3,600); E. L. Tatum, Yale University, to study new techniques of inducing new strains of bacteria, molds, etc., by means of chemical irritants ($2,500 annually for two years); W. W. Westerfeld, Syracuse University, to study the changes undergone by sugars in the animal body and the relation of such changes to the functional role of certain vitamins in the B-complex ($3,000 annually for two years); and James G. Wilson, University of Rochester, to study and analyze the malformations produced in fetal and newborn rats by maintaining the mothers on a diet deficient in vitamin A ($1,200).

The first Mary Soper Pope Medal of the Cranbrook Institute of Science, Michigan, has been awarded to Frans Verdoorn, editor of *Chronica Botanica,* in recognition of his editorial work in biology as well as for his researches in cryptogamic botany and the history of the plant sciences.

A consulting and analytical laboratory has been opened by Solomon Shankman in Los Angeles. Special emphasis is to be placed on amino acid and protein analysis. Dr. Shankman was formerly a research

associate in the Department of Chemistry, University of California, Los Angeles.

The Department of Botany, University of Nebraska, has announced several changes in its staff. On the city campus, Elda R. Walker, and Leva B. Walker, associate professors, have retired; John P. Decker, formerly of the U. S. Army, and Raymond W. Darland, recently in the Navy, have been made assistant professors; and Harry L. Weaver has been appointed as instructor. Changes in the plant pathology section on the agricultural college campus are as follows: M. W. Felton, assistant professor, has resigned to carry on commercial work; Ian W. Tervet has been appointed associate professor and associate pathologist; A. F. Sherf, assistant in pathology and assistant extension pathologist; and M. L. Schuster, instructor and assistant pathologist. R. J. pool is chairman of the Department, while R. W. Goss is chairman of Plant Pathology in the Experiment Station.

The Graduate School, University of Illinois, has established four research fellowships to be awarded for one year in the fields of medicine, dentistry, and pharmacy in Chicago at a stipend of $1,200 per year (calendar year with one month's vacation). Fellows are eligible for reappointment in competition with the new applicants. Candidates must have completed a training of not less than eight years beyond high school graduation. They should indicate the field of research in which they are interested and submit complete transcripts of their scholastic credits, together with the names of three former science teachers as references. Appointments will be announced on 1 January or soon thereafter each year. The fellowship year begins on 1 September or 1 July. Formal application blanks may be secured from: Secretary, Committeee on Graduate Work in Medicine, Dentistry, and Pharmacy, 1853 West Polk Street, Chicago 12, Illinois.

The National Malaria Society held its 29th annual meeting in Miami, Florida, on 4–7 November conjointly with the meeting of the Southern Medical Association. The program consisted of 27 papers on the parasitology, treatment, and control of malaria. Of particular interest were the reports on the new anti-malaria drugs. A special feature was the presentation of a gift from the Society to Mark F. Boyd, retiring president, for his contributions to the knowledge of malaria and its control.

A grant of $27,750 has been made to the University of Utah School of Medicine for further support of a study of muscular dystropy and other hereditary and degenerative disorders. This supplements the grant of $92,000 made last year by the U. S. Public Health Service, Research Grants Division, for the same purpose. With the aid of these funds a Laboratory for the Study of Hereditary and Metabolic Disorders has been established under the directorship of M. M. Wintrobe, professor and head of the Department of Medicine. The activities of this laboratory will be divided between three divisions: The Division of Biochemistry and Physiology, of which Francis Binkley and Emil L. Smith are in charge; the Division of Genetics, with Fayette B. Stephens in charge; and the Clinical Division. The chief of the latter division, who will also act as assistant director of the study, has not yet been selected. A metabolic ward at the Salt Lake General Hospital forms part of the clinical Division. The staff of the metabolic ward includes Virginia Davenport, formerly of the Peter Bent Brigham Hospital, Boston.

The Marine Biological Laboratory, Woods Hole, Massachusetts, is able to offer a limited number of postdoctoral fellowships in the fields of biochemistry, biophysics, and physiological chemistry, through a grant received from the Lalor Foundation. The fellowships are designed primarily for young investigators to work during the summer, making use of the facilities of the Laboratory. The stipend is intended to cover laboratory fees, travel, and living expenses at Woods Hole. Applications should be received on or before 31 January. Blanks and further information may be secured from the Marine Biological Laboratory or from the chairman of the Fellowship Committee, C. W. Metz, Department of Zoology, University of Pennsylvania, Philadelphia 4, Pennsylvania.

The Wellesley College Botany Greenhouses have recently been named in honor of Prof. Margaret C. Ferguson, head of the Botany Department from 1905 to 1930 and president of the Botanical Society of America in 1929–30, the only woman to have been so honored. The greenhouses, containing a plant collection from all parts of the world, also have space allotted for undergraduate student experimentation and for graduate and faculty research. Prof. Ferguson was retired from Wellesley in 1932 as a research professor and is now living at 1519 Allston Way, Berkeley 3, California.

The Albert Commons collection of fungi, presented to the Academy of Natural Sciences in Philadelphia following Commons' death in 1919, has now been labeled and arranged alphabetically in families, genera, and species according to the Engler and Prantl classification by David R. Sumstine, associate in botany, Carnegie Museum, Pittsburgh. The Academy is preparing proper space and purchasing boxes for

the collection of over 4,000 specimens of fungi, which mycologists will have access to in the near future. All inquiries about the use of these specimens should be addressed to: Dr. Francis W. Pennell, Curator of Plants, Academy of Natural Sciences, Philadelphia, Pennsylvania.

Union College has received a gift of $50,000 to build what is expected to become one of the Nation's most up-to-date and complete mental testing laboratories as headquarters for the Union College Character Research Project. The $50,000 grant, given anonymously by a college trustee, will provide for the physical remodeling of the interior of the North College Colonnade, built in 1814. The Character Research Project, directed by Ernest M. Ligon, has received an additional $75,000 during the past year for expansion of staff and equipment. During the past 12 years tests of character growth in hundreds of children and youths have resulted in a partial laboratory analysis of the psychological attitudes which make up wholesome and healthy human personality. During the past year activity in the project has been directed toward developing curricular materials to constitute an educational basis for the formation of those already in children through cooperation of parents, church, and public schools.

The Department of Pharmacology, School of Medicine, University of Maryland, has been awarded a $5,000 fellowship by the Emerson Drug Company, Baltimore, for the purpose of studying the mechanism of action of drugs in hypertension. Elaine Gaby is working on the problem under the direction of John C. Krantz, Jr., professor of pharmacology. The Department is also the recipient of a $5,000 fellowship from the Ohio Chemical and Manufacturing Company, Cleveland, for the purpose of studying anesthetic agents. Dorothy V. Kibler is working on this problem, also under the direction of Dr. Krantz.

Harvard University will cease to graduate Bachelors of Science from 1950 on, according to Richard M. Gummere, chairman of the Committee on Admission. The University will award only Bachelor of Arts degrees, which it has conferred since 1642, upon discontinuance of the science degree, first awarded in 1907. Dr. Gummere stated that even undergraduates majoring in scientific fields "prefer to receive the arts degree."

A gift of $25,000, to be used for the support of fundamental research, has been allocated to The Ohio State University by its Research Foundation. This supplements a grant of $100,000 made for this same purpose last year. These funds, which represent some return to the University for the use of its facilities in governmental and industrial research, will be used principally for fellowships and the purchase of specialized research equipment. The allocation of these funds to research projects will be made by the president of the University upon the recommendation of a University-wide committee, of which the dean of the Graduate School is chairman.

NRC News

The Division of Physical Sciences has reported the formation of a new Committee on High-Speed Calculating Machines, under the chairmanship of John von Neumann, of the Institute for Advanced Study, Princeton, and with the following as members: Howard H. Aiken, Walter Bartky, Samuel H. Caldwell, George R. Stibitz, and Warren Weaver. The Committee will study the principles and possibilities of high-speed automatic machines, with a view to finding ways and means for greatly increasing the speed of computations. It is contemplated that pertinent information relative to computation and current research in such machines will be distributed to interested parties.

The Division's former Committee on Standards of Radioactivity has been reconstituted as a Committee on Radioactivity. Its responsibilites have been enlarged to include work on units, standards, and measuring instruments in this field. The membership of the new Committee includes: L. F. Curtiss, National Bureau of Standards, as chairman; R. D. Evans, Massachusetts Institute of Technology, vice-chairman; Irving Feister, National Bureau of Standards, secretary; and H. L. Anderson, A. M. Brues, Martin Deutsch, A. Ghiosso, H. H. Goldsmith, P. M. Hurley, J. E. Rose, Nathan Sugarman, and W. H. Sullivan. P. C. Aebersold and T. J. Killian are liaison members for the Manhattan District and the Office of Naval Research, respectively. Work of the Committee has been distributed under several subcommittees, of which the various Committee members are serving as chairmen. One of these is to serve as a clearinghouse for collecting and distributing information and data for use of workers in the field.

Plans are maturing for the appointment of additional committees to cover other important aspects of nuclear science.

For the year 1946–47 the Division is under the chairmanship of R. Clifton Gibbs, emeritus professor of physics, Cornell University. The membership includes representatives of the American Astronomical Society (2), the American Physical Society (4), the American Mathematical Society (5), the Mathematical Association of America (1), the Optical Society of America (2), the Acoustical Society of America (2), the Institute of Mathematical Statistics (1), the American Institute of Physics (1), the Government (1), and 6 members at large.

Recent Deaths

Benjamin S. Paschall, 67, formerly professor of chemistry at Washington State University and for the past seven years president and head chemist of the Paschall Laboratories, Seattle, died on 22 November.

Frederick B. Mumford, 78, dean emeritus of the College of Agriculture, University of Missouri, died on 12 November, as the result of an automobile accident in which Mrs. Mumford also lost her life. He had been dean of the College of Agriculture from 1909 to 1938 and dean emeritus since the latter date.

Charles Needham Forrest, 70, retired chemical engineer formerly with the Barber Asphalt Corporation of Perth Amboy, New Jersey, died in Fort Myers, Florida, on 2 December.

James Henry Leuba, 78, professor emeritus of psychology at Bryn Mawr, died at Winter Park, Florida, on 8 December. Among Dr. Leuba's books are: *The psychological origin and the nature of religion, A psychological study of religion, The belief in God and immortality,* and *The psychology of religious mysticism.*

Henry A. Trautman, 54, head of the Trautman Chemical Engineering Company, Cleveland, died on 3 December.

In the Laboratory

Photographic Measurement of Radiation Quality and Quantity

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and

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It is recognized authoritatively that the degree of ionization produced by X-rays is a relative measurement of quantum energy, the intensity of which is expressed as the number of roentgens per unit time (*6*). For a beam of radiation having a given intensity, a quality index of the degree of ionization produced, or the amount of energy absorbed, in a unit mass is expressed as the relative absorption in various thicknesses of a material (usually full absorption curves in Cu or Al), a simplified value of which is the HVL (thickness of material that reduces the ionization to one half). The biologic effect is thus expressed as the exposure in roentgens (intensity × time) to radiation of a given tissue absorbability.

To date, the standard free-air ionization chamber has been accepted as the most accurate instrument for measurement of radiation quality and intensity. According to the definition of the roentgen, the only requirement of an X-ray measuring instrument is that it indicate the same number of r's per unit time as the standard air chamber when placed at the same point in a suitably defined beam (*11*). The principles of the free-air chamber have been recently extended to the development of the thimble-type chamber, the wall of which is of a material approximating human tissue in density and X-ray absorption. Its accuracy is dependent on calibration with the free-air chamber and the conditions under which it is used. Because extensive laboratory equipment is not required, this instrument is readily employed for the measurement of small doses of scattered and direct radiation in field studies.

The photographic effects of X-rays have been studied extensively as a basic science since their discovery in 1895. Most of these studies were based on the Bunsen and Roscoe reciprocity law, E = It (*5*), and the Hurter and Driffield characteristic curve relating density and the logarithm of exposure (*10*), which had been reported previously for visible light. Barkla and Martyn (*1*) in 1913 concluded that the photographic effect produced by X-ray beams of a given intensity varied with the wave length—the more penetrating the radiation, the smaller the photographic effect. This was confirmed by Berthold and Glocker, Bouvers, and Bell (*2–4*). Bell also showed that, if development variables are eliminated and intensifying screens are not used, the shape of the H & D curve is independent of quality; under these conditions the failure of the reciprocity law was found to be negligible (10 per cent or less for an intensity range of 1–10,000). Bell and Henny, (*2, 8*) found that, unless intensifying

[1] The authors express their gratitude to A. S. Gray and W. H. Weidman for making this paper possible; acknowledgment with thanks is made to the Machlett Laboratories, Springdale; United Aircraft Corporation, East Hartford; and the Hartford and St. Francis Hospitals, Hartford, for the use of radiation equipment during the course of this study.

screens are used, the "intermittency effect" is also negligible. Preliminary work by the present authors confirmed these findings. It was concluded that, if a "characteristic curve" representative of the material and development employed is available for a specific quality of radiation, such a curve can be used to determine accurate relative intensities from film blackening when the densities corresponding to the film blackening and the "characteristic curve" are read on the same densitometer or on similarly calibrated instruments. Also, when the effect of quality on film blackening is known, such a curve may be used to determine accurate relative intensities of radiations of varying quality.

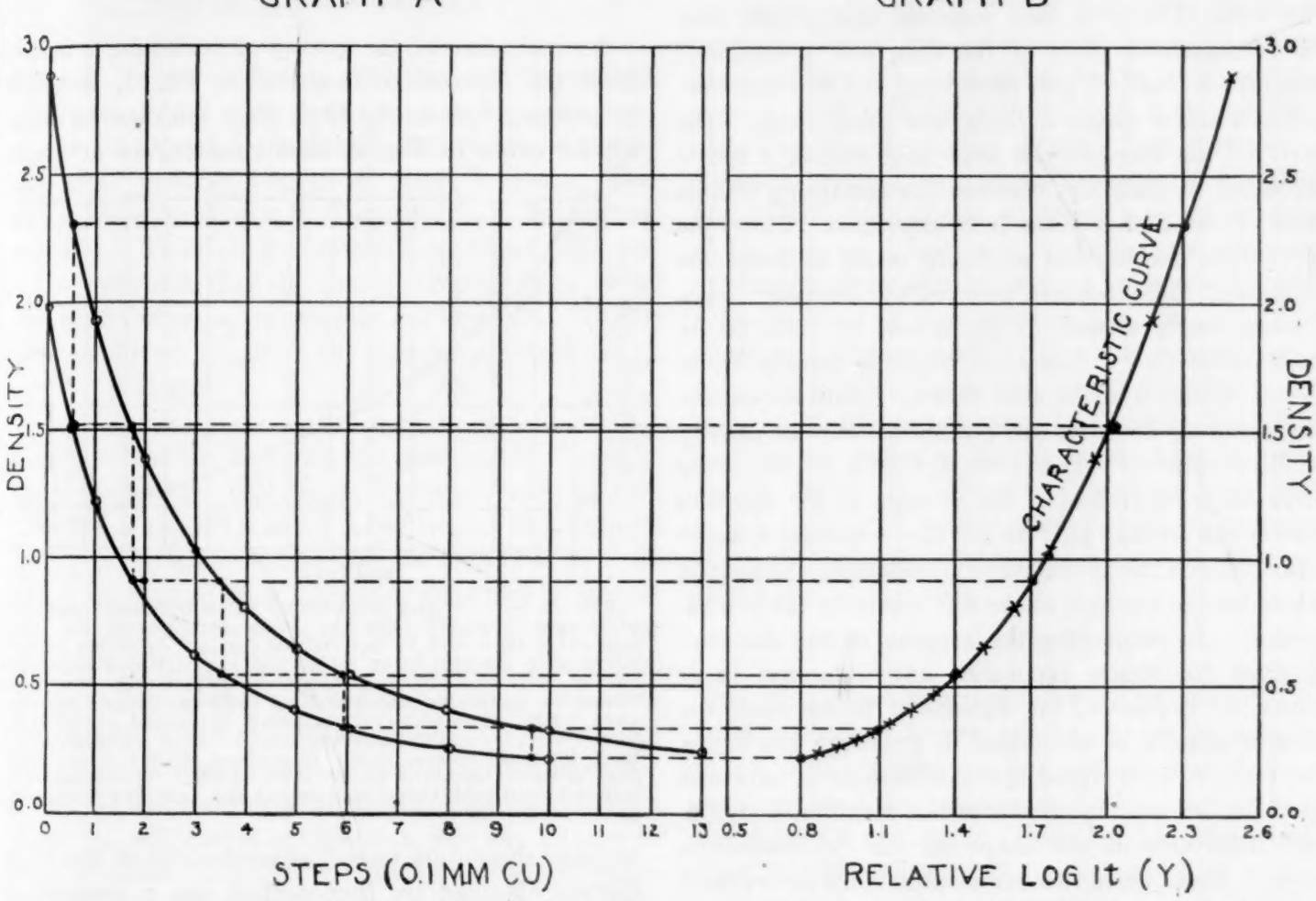

FIG. 1. *Graph A*—Densities obtained under step tablet: lower curve = average of densities produced by single exposure; upper curve = densities produced by cumulation of two exposures; ○ = densities obtained under various tablet steps; ● = construction points for characteristic curve; vertical dotted lines represent the density increment for 0.30 *log It* at the designated points. *Graph B*—● = construction points, placed on ordinates 0.30 *log It* apart, for characteristic curve, corresponding to similar points on the curves of Graph A and connected with them by interrupted lines to show the graphic construction employed. For convenience in graphing, a density of 1.5 and a *relative log It* of 2.0 were used as standard points of departure. × = densities produced under 0.1 mm. thickness of Cu varying from 0.0 to 1.3 mm. and corresponding to the *relative log It* values used for the construction of the photoabsorption curve (Fig. 2).

To date it has been difficult to duplicate the conditions under which a "characteristic curve" may be determined. For this reason intensity values derived from film blackening have not been sufficiently accurate for comparative measurement of radiation quality and quantity unless extensive laboratory control is applied. A vast amount of sensitometric data has accumulated through many researches, both from the point of view of general radiography (*9, 12*) and the use of films for radiation measurement (*2, 8*). These authors have shown that quantitative errors seldom exceed 5 per cent if films of the same type and emulsion number are developed simultaneously; however, a discrepancy up to 30 per cent was reported if the films are developed at different times, and this error may be increased to 50 per cent or greater if films of different emulsion numbers are used. These errors were found when the conditions of development were supposedly similar. Henny (*8*) has shown that films of the same emulsion number, developed for 6 instead of 5 minutes, may show an error as great as 100 per cent. The present authors found errors of similar magnitude in earlier experiments.

A simple method for determining the "characteristic curve" (v.s.) under routine conditions was developed from previous investigations by one of us (J.K.) for the photometric calibrations of X-ray equipment. The authors report herein the application of the principles of the method in the measurement of radiation quality

and quantity in terms equivalent to presently accepted methods.

Determination of a Representative "Characteristic Curve"

A metal stair tablet is placed over the film (thickness 0 included), a lateral third of which is covered by a lead mask, and an exposure, *It* (*I* = intensity, *t* = time), in roentgens measured by a r-meter is made. The strip of lead is then removed and placed over the contralateral third of the film, and a duplicate exposure is made. Upon processing, the film thus furnishes a tablet image divided into three zones. The parts of the film covered with lead receive a single exposure, respectively, whereas the remaining middle third of the film receives both exposures. Thus, the latter zone receives an exposure equal to twice the average of the exposures received by the other zones. The exposures should be so chosen by trial or by known data that a maximum readable density is obtained on step 0 in the zone receiving both exposures. The resulting densities are plotted directly as density vs. filter thickness curves (Fig. 1, Graph A), the lower curve being equivalent to the average of the densities determined in that part of the film receiving a single exposure, and the upper curve representing the density determined in the part of the film receiving the two exposures. In employing the average of the densities obtained for single exposures, any difference in *It* caused by failure of the equipment to duplicate exposures exactly is minimized in graphing the curve. The authors have found that a difference in exposure up to 10 per cent usually does not result in a significant difference in the shape of the "characteristic curve." From these two curves points are determined, 0.30 *log It* apart corresponding to the density increment produced either by halving or doubling the exposure. A "characteristic curve," density vs. *relative log It,* is determined as shown in Fig. 1, Graph B. This curve is similar to an H & D (density vs. log time) curve, and is of the same shape, assuming no failure of the reciprocity law. It is characteristic of the material, developing process, and densitometer used. Cumulative errors involved in the determination of this curve were found to be small. Curves obtained from exposure of films of the same emulsion number to varying dosages and qualities of radiation were found to match within 0.02 *log It* within the range of densities between 0.30 and 3.0, a variation found to be within limits satisfactory for most practical purposes. It is thus possible to determine an unknown dosage, *x,* in r's from the film blackening produced by an X-ray beam of normal incidence and of the same quality as that employed in exposing the film used for the determination of the "characteristic curve" by the equation:

$$x = s\,[\text{antilog}\,(Y_x - Y_s)], \qquad (1)$$

wherein *s* is the dosage in roentgens given this film, and Y_x and Y_s are the *relative log It* values, corresponding to the film densities produced by *x* and *s*, respectively, as determined from the "characteristic curve" for the film and processing employed.

Determination of Quality

An indication of the quality of radiation is derived from the "characteristic curve" in Fig. 1, Graph B, by plotting *relative log It* vs. filter thickness as shown by the curve in Fig. 2, thus resulting in a "photographic absorption curve" characteristic of the beam. Curves obtained by this method are a measure of variation in photographic effect only, and are not directly comparable with ionization absorption curves. It has been shown by Glasser (*7*), and confirmed in our experiments, that the relationship between photographic and ionization effects changes with the wave length. However, it is reasonable to assume that the two types of curves bear a definite relationship, and that they can be transposed from one type to the other when the ratio "photometric intensity/ionometric intensity" for given conditions is known.

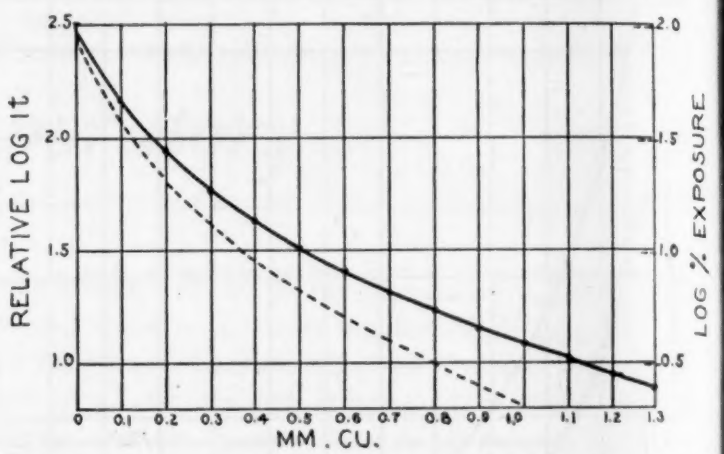

FIG. 2. ——= photoabsorption curve obtained from data of Graphs A and B, Fig. 1. From such curves the photo half-value layer can be determined for any filtration as compared with the ionization HVL from conventional absorption curves: PQI is 0.110, and the photo HVL, 0.092. Curve obtained at approximately 100 KVP full-wave valve rectification, 1 mm. Al total filtration, using ultraspeed dental X-ray film. – – – – –= photoabsorption curve of standard beam used in experiments, using ultraspeed dental X-ray film; PQI is 0.088, and the photo HVL, 0.068. The same curve was obtained with slow-speed dental film and slow-speed, fine-grain industrial film.

It was found that the slope of this quality curve might be expressed conveniently in an approximate half-value layer to which is applied the term "photographic quality index." This index is derived from the HVL formula, the thickness of filter in millimeters to reduce the intensity of a beam by one half, *i.e.* $\frac{I_o}{I_m} = 2$, where I_o is the incident radiation intensity, and I_m is the intensity of the beam after passing

through filter thickness, m. For monochromatic radiation following the law, $I = I_o e^{-nd}$, the HVL can be calculated from the equation:

$$\frac{m \log 2}{\log \frac{I_o}{I_m}} \quad \text{or} \quad \frac{0.30\ (m)}{\log I_o - \log I_m}. \qquad (2)$$

Similarly, the quality of a beam is referred to by its photographic quality index:

$$\frac{m \log 2}{\log \frac{(\text{photointensity at o})}{(\text{photointensity at m})}} \quad \text{or} \quad \frac{0.30\ (m)}{Y_o - Y_m}, \qquad (3)$$

where Y_o is the *relative log It* value for the density under step 0, *i.e.* without filtration, and Y_m the *relative log It* value for the density caused by the radiation after passing through m filter thickness. The straight-line function is thus assumed for heterogenous radiation. This assumption has been found valid for a first approximation of quality ranging from 60 to 250 KVP when m represents 0.2 mm. Cu. Under these conditions Equation (3) may be expressed as:

$$\frac{(0.2) \log 2}{Y_o - Y_{0.2\text{ mm. Cu}}} = \frac{0.06}{Y_o - Y_{0.2\text{ mm. Cu}}}. \qquad (4)$$

It is felt that the value of this photographic quality index, designated PQI, is of the same order of significance as the HVL of an X-ray beam. It is derived from photographic effects, whereas the HVL, by definition, is obtained from intensities measured by ionization effects. It is recognized that the PQI per se, as is true with the HVL, does not furnish a complete description of quality. Two X-ray beams of the same PQI might, under certain conditions, vary markedly in quality; nevertheless, two other X-ray beams of the same PQI value are of approximately the same quality when the differences in filtration are not great. It may be added here that the photographic half-value layer, *i.e.* the filtration which reduces the photographic effect by one half, may be obtained from the photoabsorption curve (Fig. 2) or more directly from the curves in Fig. 1, Graph A. The procedure requires two controlled exposures and the graphing of the determinations of film blackening under a minimum of three steps, including steps 0, 0.1, and 0.2 mm. Cu. However, the PQI can be obtained by a single exposure involving the determination of film blackening produced under two steps, *i.e.* 0 and 0.2 mm. Cu, when the "representative characteristic curve" is known. This markedly simplifies the procedure when a number of measurements are to be made. The PQI has proved as satisfactory as the photographic half-value layer within the general accuracy obtained in dosage measurement by the method here presented.

Determination of Dosage

An X-ray beam of a given quality will produce a given photographic effect. The resultant film blackening will depend on the type of film and the development conditions. Assuming no failure of the reciprocity law, if the beam quality is kept constant and the development conditions are controlled, film blackening is dependent only on exposure *It*. Under these conditions, the degree of film blackening produced by a known exposure in roentgens can be empirically determined. It is then possible to interpret film blackening as greater or less than a known exposure in roentgens. However, if the "characteristic curve" representative of the material and development conditions and the film blackening due to an exposure to a given dose in r are known, then it is possible to translate film blackening directly into roentgens by Equation (1). However, with beams of a different quality this value of x is no longer a direct expression of the dose in r, since the number of r's required to produce a given film blackening varies with quality.

For a beam of a given quality, *a*, the density produced by a known exposure in r is represented on the curve by *relative log It* (a) or Y_a. Similarly, for a beam of a different quality, *b*, the density produced by the same exposure in r is represented by *relative log It* (b) or Y_b. Since the "characteristic curve" is independent of quality, then $Y_a - Y_b$ represents the log of the ratio of the photographic effects, P_a and P_b, of the two beams, *i.e.*

$$\log \frac{P_a}{P_b} = Y_a - Y_b. \qquad (5)$$

Thus, film blackening produced by an unknown dose from a beam of known quality, *b*, can be translated into r value upon comparison with the film blackening produced by a known dose in r of a beam of known but different quality, *a*. Equation (1) thus resolves itself into the following:

$$X_b = \frac{P_a}{P_b} S_a\ [\text{Antilog}\ (Y_{x_b} - Y_{s_a})], \qquad (6)$$

where X_b is the unknown dosage of beam quality *b*, and S_a the known dosage of beam quality *a*.

When a beam of quality *a* is used as a standard, and the photographic effect, P_a, is considered as unity, then $\frac{P_a}{P_n} = \frac{1}{P_n}$, wherein P_n is the photographic effect of a beam of any quality. The values of $\frac{1}{P_n}$, when determined for beams of different quality in comparison with the standard beam, can be used as coefficients for quality *Cq*. The equation then becomes:

$$X = Cq\ (s)\ [\text{Antilog}\ (Y_x - Y_s)], \qquad (7)$$

where *Cq* is the proper coefficient for the quality of the beam used for the unknown exposure, and *s* is the value in r of the exposure made with the beam of standard quality.

The authors have determined the *Cq* for beams of

various qualities expressed in PQI, using a standard beam (80 KVP, fully rectified, 1 mm. Al total filtration, and a PQI value of 0.088). *Cq* for PQI values ranging from 0.060 to 0.300 are shown in Fig. 3. The graph is only a first approximation; these values will probably require correction dependent on additional experimental work with varying KVP and filtration. Employing the *Cq* values derived from this graph as correction factors in Equation (7), the authors tested the accuracy of the photographic method by simultaneous exposure of film and a thimble-ionization chamber (condenser r-meter). Direct radiation at a right angle to the film, varying in kilovoltage from 60–250 KVP and in dosage from 0.05–5.0 r, was used for this purpose. In a series of 53 observations to date the mean of the difference in r values between the ionization and photographic measurements as obtained in individual tests was 5.6 ± 1.2 (S. D. of the mean) per cent.

Preliminary work with both direct and scattered radiation at other than normal incidence indicates that a similar accuracy can probably be obtained under these conditions when experimentally determined correction factors for angle of incidence and scattering are used. Details of this work, and the practical application of the photographic method in personnel monitoring and X-ray machine calibration will be reported in a subsequent paper. The authors recognize that the ionization chamber affords the most accurate method for radiation dosage determination. The small number of trial tests (75 to date) made with the photographic method herein described do not permit thorough evaluation. However, the relative accuracy of the method is encouraging. It is felt that further investigation is warranted because of the simplicity, inexpensiveness, and convenience of the method. The method is particularly adaptable to the determination of exposure of personnel to radiation for prolonged periods, including the approximation of the quality of radiation received, the calibration of equipment with a minimum of test exposures, and the standardization of radiographic technics.

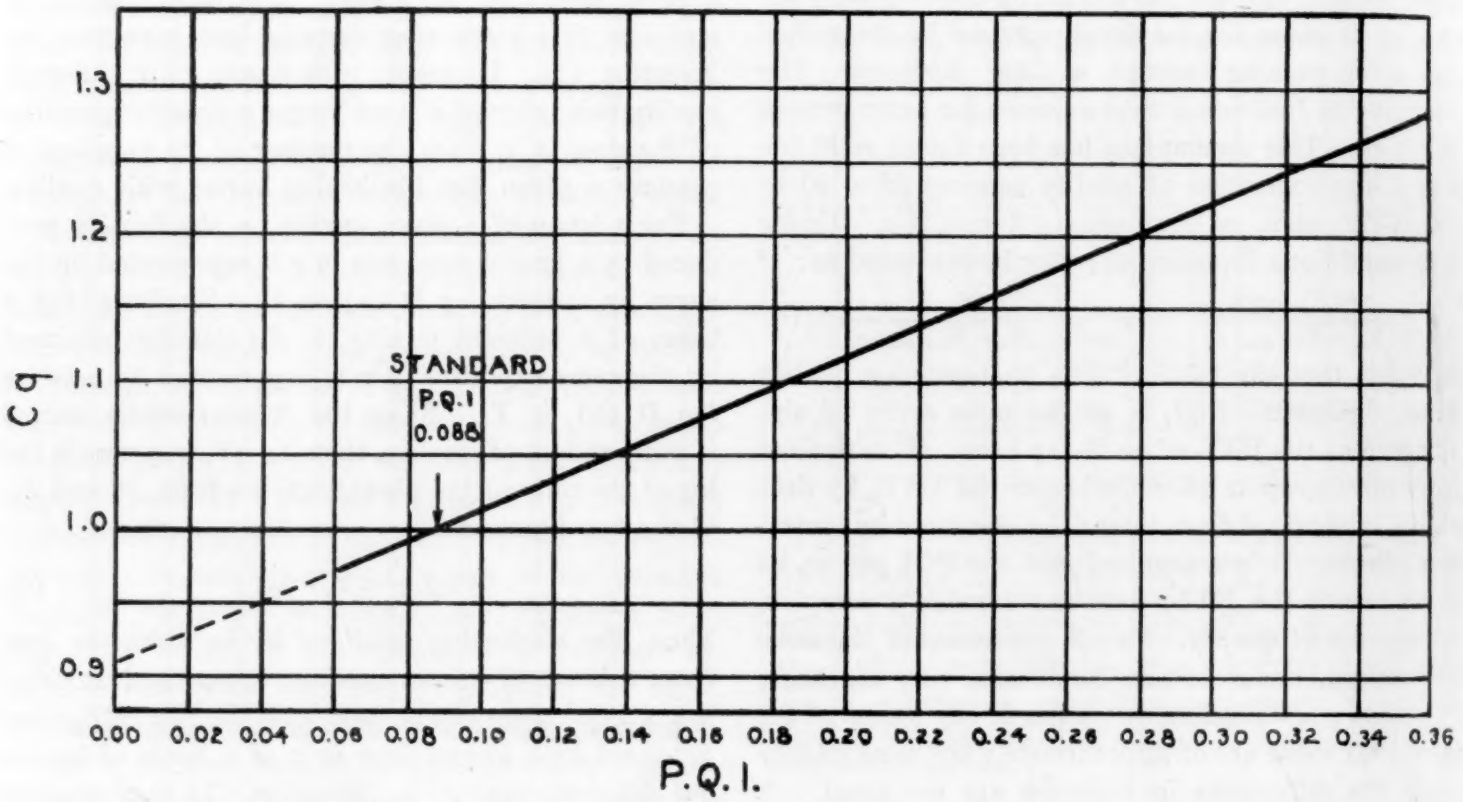

FIG. 3. Relation of correction coefficient for quality *Cq* and photoquality index, PQI, for determination of dosage from film blackening; actual values shown in graph are those for a standard beam of 0.088 PQI; coefficient values for any other beam used as control can be found by using the ratio: $\frac{C_q \text{ for tested beam}}{C_q \text{ for control beam}}$; graph values approximate only, probably accurate within 5 per cent for PQI values from 0.06 to 0.36.

References

1. BARKLA, C. G., and MARTYN, G. H. *Phil. Mag.*, 1913, **25**, 296.
2. BELL, G. E. *Brit. J. Radiol.*, 1936, **9**, 578.
3. BERTHOLD, R., and GLOCKER, R. *Z. Phys.*, 1925, **31**, 259.
4. BOUVERS, A. *Acta Radiol.*, 1925, **4**, 368.
5. BUNSEN, R., and ROSCOE, H. E. *Phil. Trans. roy. Soc.*, 1863, **153**, 139.
6. GLASSER, OTTO. Measurement of quantity by thimble chambers. In *Medical physics*. New York: Yearbook Publishers, 1944. P. 1370.
7. GLASSER, O., and ROVNER, L. E. *Radiology*, 1934, **22**, 309.
8. HENNY, G. C. *Amer. J. Roentgenol. rad. Therapy*, 1941, **9**, 895.
9. HODGSON, M. B. *Amer. J. Roentgenol.*, 1917, **4**, 610.
10. HURTER, F., and DRIFFIELD, V. C. *J. Soc. Chem. Ind.*, 1890, **9**, 455.
11. VICTOREEN, J. A. Measurement of quantity by thimble chambers. In *Medical physics*. New York: Yearbook Publishers, 1944. P. 1370.
12. WILSEY, R. B. *Amer. J. Roentgenol. rad. Therapy*, 1934, **32**, 789.

The Use of Unsaturated Polyester Resins for Embedding Biological Material

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A process for the volume production of biological materials embedded in plastic has been developed, utilizing an unsaturated polyester resin[1] found to be especially suited for soft and delicate forms such as embryos, jellyfish, cartilaginous skeleton parts, and flukes.

Several experimenters have published reports on successful methods for embedding biological materials (*1*), but material suitable for quantity production has not been a significant factor in this research.

Thus, the problem was twofold: (1) to find a plastic material suitable for quantity production, and (2) to provide plastic preparations of clarity and durability for educational purposes.

In methods described by other experimenters most of the work had been done with monomeric methyl or ethyl methacrylate and some with polymeric powders and combinations of monomeric liquids and polymeric powders. Monomeric styrene also has been used.

[1] "Selectron"—Pittsburgh Plate Glass Company.

The methacrylates, although unsurpassed in clarity, have properties which are serious drawbacks to their application.

After considerable work our efforts were concentrated on Selectron, which was found to be the most practicable from the standpoint of handling soft and delicate forms. Moreover, the plastic clears the specimens, making them transparent and the internal structure visible.

The process following was adapted from the technique employed in preparing microscope slides, to the point of bringing together the specimens and plastics.

(1) The specimens may be fixed in Bouin's fluid, formaldehyde, or any of the usual fixatives. All fixatives, regardless of the type used, must, however, be completely removed. In the case of Bouin's, which is customarily used on embryos, the picric acid must be eliminated by washing in several changes of 70 per cent alcohol. The first few changes should contain a small amount of saturated aqueous lithium carbonate. After all the yellow color has disappeared, the specimens should be transferred to water. Formaldehyde may be removed by washing in water.

(2) After the specimens are washed in water, they are stained in acid carmine to a point where internal structures are completely stained. Destaining is then carried to a point where the specimen is pink, since

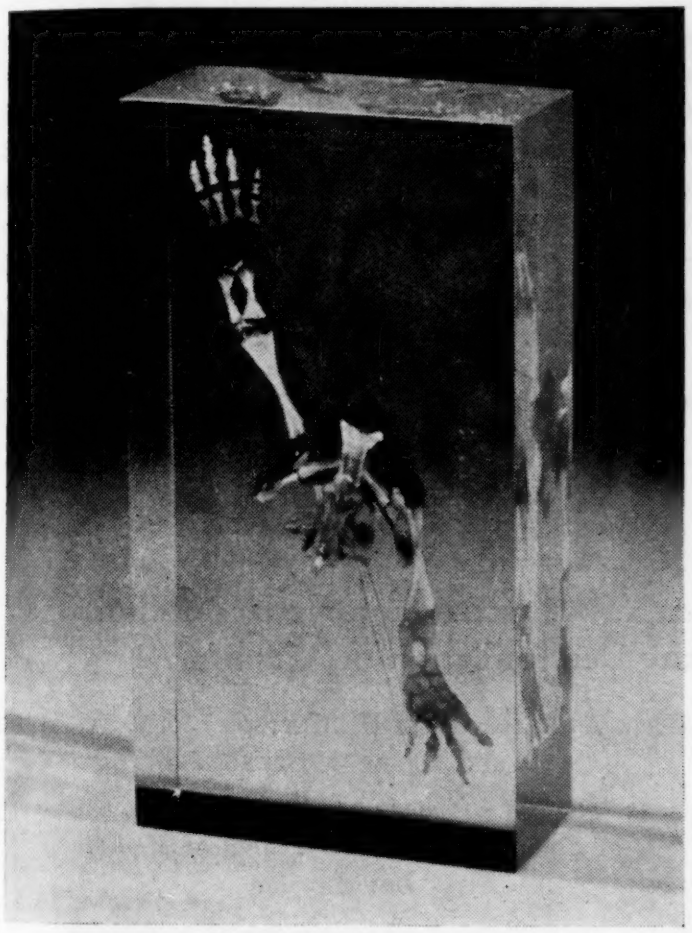

FIG. 1. Necturus pelvic girdle and limbs.

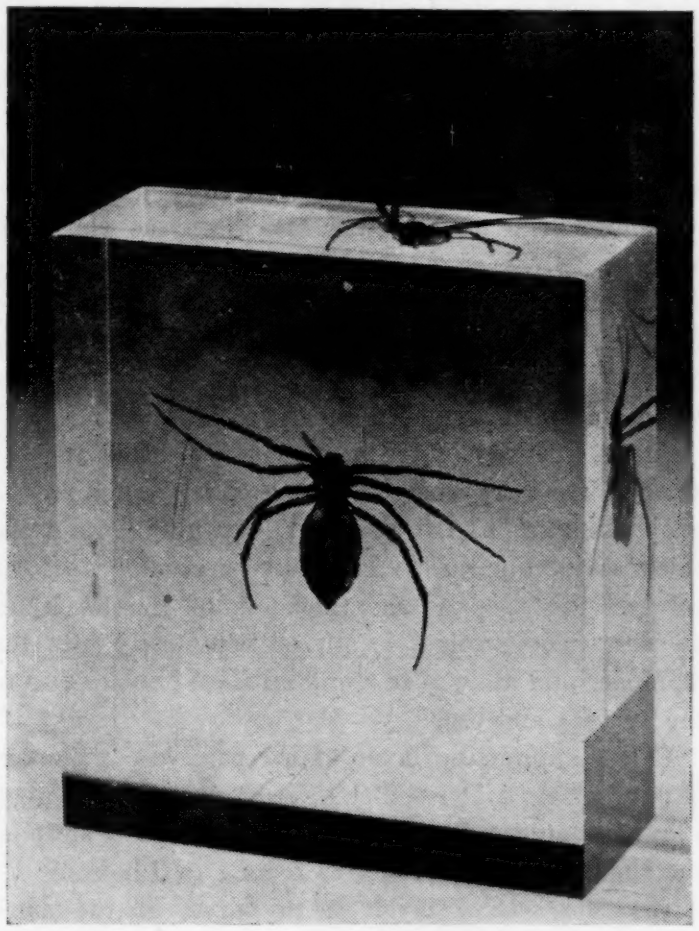

FIG. 2. Garden spider.

the plastic intensifies the color. Hematoxylin has been tried, but has not produced a satisfactory stain. The difficulty lies in adjusting the intensity of the stain, which is increased by the plastic.

(3) The specimens are dehydrated in a series of alcohols (70, 83 and 95 per cent and absolute), the time depending upon the size of the specimens.

(4) The next stage of the process—removing the alcohol—presented many difficulties. At first, various compatible solvents were tried, but these proved unsuccessful. The plastic in and around the specimens was diluted, producing internal strains resulting in cleavages and fractures in the blocks. To overcome this, the specimens are transferred from absolute alcohol to anhydrous ether. Here again the time is varied from an hour for early chick embryos to several hours for larger specimens. The anhydrous ether displaces the alcohol and removes any traces of water from the specimen.

(5) The specimens are next transferred into the uncatalyzed plastic and evacuated in a vacuum desiccator to draw off the ether and allow the plastic to impregnate the specimen. This must be done very slowly and carefully until a vacuum is produced (500–700 mm. of Hg.) and left to stand until all the ether has evaporated. Too rapid evacuation causes the ether to boil, destroying the specimens.

(6) A quantity of the monomer is weighed and the catalyst (tertiary butyl hydroperoxide) added in the proportion of 0.1–0.5 per cent, depending upon the thickness of the block. The lesser percentages of the catalyst are used as the thickness of the block increases. The catalyst is stirred completely into the monomer and allowed to stand until all bubbles rise to the surface and break.

(7) A supporting layer of the catalyzed monomer is poured into a Pyrex dish or tray and allowed to gel at room temperature, until it is firm enough to support the specimens. This requires from 1 to 3 hours.

(8) The second layer is prepared in the same manner and poured onto the first.

(9) The specimens are transferred from the uncatalyzed monomer to the trays, care being taken to carry over as little as possible, and are then oriented on the first layer.

(10) The trays are left to stand at room temperature until the second layer has gelled.

(11) After the gelation is complete, the trays are placed in an oven to cure for approximately 2–4 hours. The heat is raised slowly from 100° F. to 250° F. and maintained at 250° F. for ¼–1 hour.

(12) After cooling, the blocks are easily removed by merely inverting the trays and allowing the blocks to drop out.

The plastic, being thermosetting, does not require any elaborate or special equipment for cutting or polishing. A fine-toothed band saw is used for trimming and cutting, while polishing is done on a soft-rag wheel using tripoli and rouge.

The process, as outlined above, has worked successfully on chick embryos, pig embryos, jellyfish, flukes, and other similar forms. While no extensive experimental work has been done on forms which may present different problems, we feel confident that in time these other forms can be embedded in this type of resin.

In general, the unsaturated polyester resins are a light-yellowish color, but some of these are available in a purified form; while not as water-white as the methacrylates or styrene, these have the advantage of a much simpler curing schedule. Also, the polyesters are more resistant to abrasion than the methacrylate. Occasionally, the blocks will have to be repolished. This can be done easily on a soft-rag wheel or by hand, using pumice paste, finishing with rouge, and then wiping with a waxed cloth. It will be found that by using a little care in handling, much unnecessary work can be avoided.

Reference

1. KNIGHT, H. G. *Science*, 1937, **86**, 333–334; PUCKETT, W. O. *Science*, 1940, **91**, 625–626; STRUMIA, MAX M., and HERSHAY, J. IVAN. *Science*, 1944, **99**, 105–106; ———. Technical Service Report No. 4, 1 February 1945, E. I. Du Pont de Nemours & Co.; ———. Embedding specimens in methacrylate resins. (U. S. Department of Agriculture Bulletin.)

A New Spectrophotometric Method for the Determination of Vitamin A[1]

JORGE AWAPARA, FRED H. MATTSON, JOHN W. MEHL, and HARRY J. DEUEL, JR.

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The spectrophotometric determination of vitamin A is not generally applicable to materials low in vitamin A and containing appreciable amounts of other nonsaponifiable materials (*2*). In an attempt to develop a method which would be suitable for the determination of vitamin A from tissues of vitamin A-depleted animals, we have examined the possibility of purifying the nonsaponifiable fraction by chromatographic methods before spectrophotometry. We wish to report briefly on the difficulties encountered in chromatography, the use of floridin in vitamin A analyses, and the application of this technic to margarine.

[1] This work was supported by a grant from the Nutrition Foundation.

Adsorption of the nonsaponifiable fraction from petroleum ether solutions has been studied, using MgO according to the method of Wilkie and DeWitt (*4*) and alumina columns. In all instances difficulties were experienced in obtaining satisfactory chromatograms when margarines or vegetable oils containing vitamin A were used. It was found that sufficient sterols were present in the petroleum ether extract of the nonsaponifiable fraction to act as an eluting agent and thus prevent the formation of sharp rings which could be observed in ultraviolet light. Interference due to the sterols could be avoided by treatment of the nonsaponifiable extract with digitonin or by chilling the extract in methanol in a mixture of dry ice and ethyl alcohol and filtering before chromatography. Subsequent chromatograms were sharp, but material subsequently removed from the column by elution or by cutting the column did not give a typical vitamin A curve. The interfering material appeared to consist of tocopherols and their breakdown products, and we have not been able to achieve any satisfactory separation of these compounds from vitamin A on such columns.

Although moderately satisfactory results could be obtained by correcting the spectrophotometric curves for the tocopherols estimated from the extinction at 293 mμ, we felt that it would be worth while to explore the possibilities of floridin (floridin XXS, 60–80 mesh),[2] which has been employed to remove vitamin A and sterols from tocopherols (*1*). Although we were able to confirm the observation that vitamin A can be quantitatively adsorbed from floridin with benzene, and the tocopherols quantitatively recovered in the filtrates, we have been unable to recover the vitamin A from the floridin. This is doubtless due to the reaction which takes place on floridin (*3*). Since vitamin A is the only material having an absorption between 300 and 350 mμ which is adsorbed on floridin, this treatment offers a method for differential determination of vitamin A.

The following method has been applied to margarines and vegetable oils. A 5-gram sample is saponified for 30 minutes with 5 ml. of 50 per cent KOH and 20 ml. of 95 per cent ethyl alcohol. The hydrolysate is made to a total volume of 80 ml. with water and alcohol to give a final alcohol concentration of 50 per cent. Extraction is carried out for 3½ hours with 120 ml. of Skellysolve A in a continuous extracter. The petroleum ether extract is washed twice with water, three times with 0.5 per cent sodium hydrosulfite, and four times more with water. The petroleum ether is then removed by evaporation in a stream of nitrogen, and the residue is taken up in 10 ml. of benzene. Five ml. of this solution are diluted to 25 ml. with benzene, and the spectrophotometric measurements are made at 300, 332, and 350 mμ. The remaining 5 ml. of benzene solution are poured onto a layer of purified floridin, 4 mm. thick, in a chromatographic column, 20 mm. in diameter. The floridin is first wet with 5 ml. of benzene and the extract added carefully before the benzene has disappeared from the column. (When considerably thicker layers of floridin were used, it was found that substances other than vitamin A were removed from the extract and the results were inaccurate.) The column is then washed with about 15 ml. of benzene, the combined washings are made up to a volume of 25 ml., and readings made on the spectrophotometer at the wave lengths indicated above. The calculation of vitamin A concentration is made from the difference between the readings for the two solutions at 332 mμ, and the differences between the readings at 300 to 350 mμ serve to demonstrate the completeness of removal of the interfering substances (Fig. 1). In calculating the vitamin A it must be remembered that its absorption curve in benzene dif-

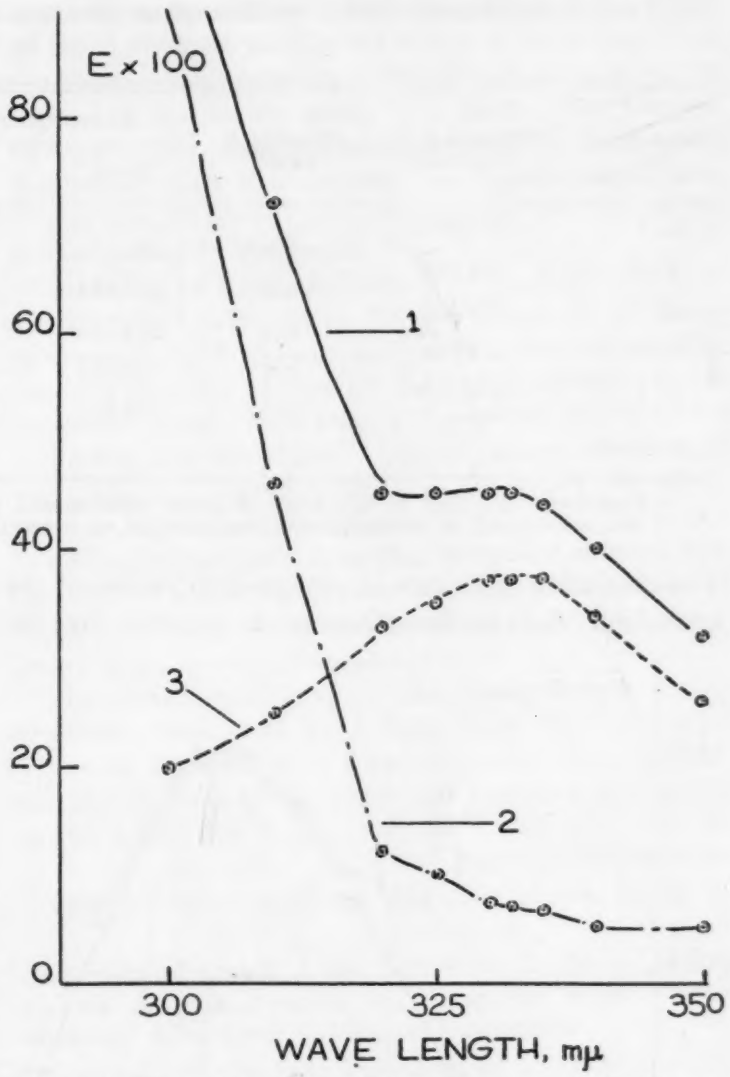

FIG. 1. The extinction (× 100) of the nonsaponifiable extract of margarine in benzene (Curve 1), of same extract after floridin treatment (Curve 2), and of vitamin A obtained by difference between Curves 1 and 2 (Curve 3).

[2] Obtained from the Floridin Corporation, Warren, Pennsylvania. This was purified as described by Emmerie and Engel (*1*).

fers from the curves in petroleum ether or alcohol, and we have used the relation

$$\text{Vitamin A in I.U./gram} = \frac{(\text{extinction difference at } 332\ \text{m}\mu)\,(50)}{0.0442\ (\text{weight of sample})}.$$

solved; the factor 0.0442 is the value taken for the extinction of a solution containing 1.0 I.U./ml. This factor is based on the usual conversion figure of 2,000, corrected for the difference between the absorption in benzene at 332 mμ and petroleum ether at 328 mμ.

TABLE 1

THE VITAMIN A CONTENT (I.U.) OF MARGARINE AS DETERMINED IN SUCCESSIVE DETERMINATIONS WITH THE FLORIDIN TECHNIC BASED ON THE $E^{1\%}_{1\ CM.}$ AT 332 mμ

Sample No.	Vitamin A in 5 grams	Vitamin A added	Extra vitamin A recovered		Margarine vitamin A/pound	
			Total	%	Uncorrected	Corrected average
1, 1	151,169	191*	159,171	83.3, 89.6	13,700, 15,300	16,800
1, 2	161,165	245	200,214	81.6, 87.3	14,600, 15,000	17,600
2, 1	156,159	254	209,219	82.3, 86.3	14,200, 14,400	17,000
2, 2	154,161	257	180,212	70.1,† 82.5	14,000, 14,600	17,300
2, 3	166,170	255	217,231	85.2, 90.5	15,100, 15,400	17,300
Average				85.4	14,630	17,200

* Fish-liver oil added in this test; in other experiments, pure vitamin A alcohol was used.
† Not considered in average or in calculation of corrected average of margarine vitamin A.

The extinction difference is presumed to represent the extinction due to the vitamin A removed by the floridin; the factor 50 corresponds to the final total volume in which the nonsaponifiable fraction is dissolved; the factor 0.0442 is the value taken for the extinction of a solution containing 1.0 I.U./ml. This factor is based on the usual conversion figure of 2,000, corrected for the difference between the absorption in benzene at 332 mμ and petroleum ether at 328 mμ.

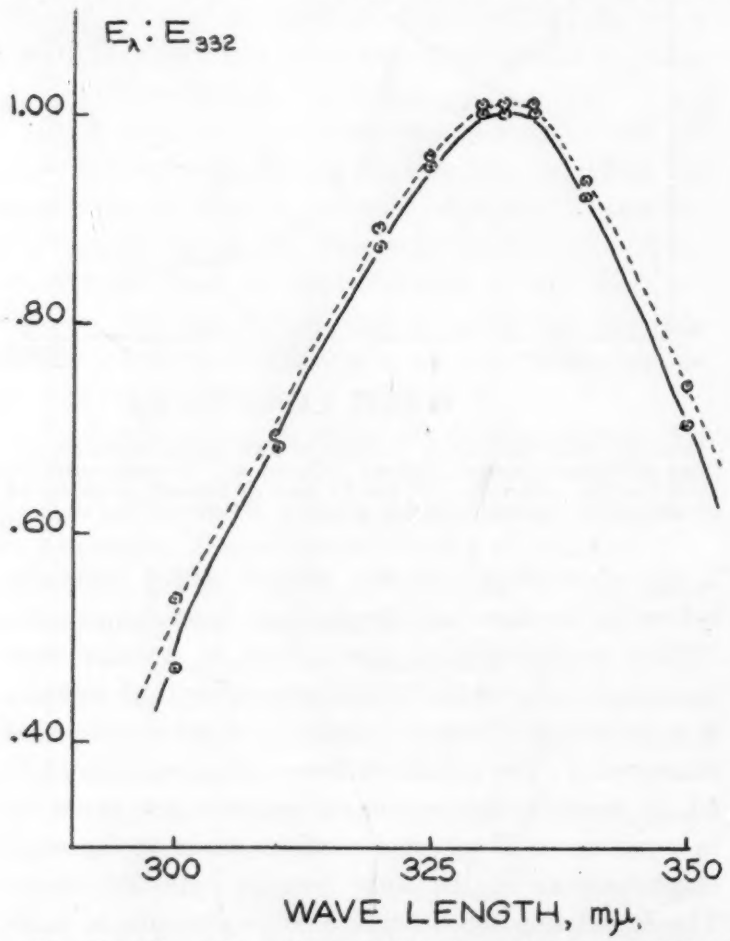

FIG. 2. The ratio of E_λ to E_{332} for vitamin A alcohol (Distillation Products) in benzene (solid line) and for margarine "vitamin A" obtained by difference between absorption of untreated nonsaponifiable fraction and fraction treated with floridin (dotted line).

The validity of the method may be judged by the identity of the difference curves for the "vitamin A" of margarine determined by this procedure and for vitamin A alcohol (Fig. 2).

That the method is satisfactory is also indicated by the uniformity of the uncorrected values for vitamin A in the different samples of margarine. These unselected results obtained on consecutive days indicate that the results are reproducible. Although the corrected figures for vitamin A are based on a recovery factor of only 85 per cent, it is believed that by better extraction procedures this can be considerably improved. However, with the present method using a standardized procedure, a determination with a probable error of ±2 per cent is available after correction for recovery obtained with added vitamin A.

Addendum. With more efficient extractors which we are now employing, we have been able to obtain consistent recoveries of better than 95 per cent of added vitamin A. Uncorrected values for vitamin A in margarine with the new equipment were found to average 18,200 I.U./pound.

References

1. EMMERIE, A., and ENGEL, C. *Rec. trav. chim.*, 1939, 58, 283.
2. SEXTON, E. L., MEHL, J. W., and DEUEL, H. J., JR. *J. Nutrition*, 1946, **31**, 299.
3. TAKAHASHI, K., and KAWAKAMI, K. *J. chem. Soc. Japan*, 1923, **44**, 590; MEUNIER, P. *C. R. Acad. Sci., Paris*, 1942, **215**, 470; LOWMAN, A. *Science*, 1945, **101**, 183; KREIDER, H. R. *Science*, 1945, **101**, 377; ZECHMEISTER, L., and SANDOVAL, A. *Science*, 1945, **101**, 585; MAYER, G. G., and SOBOTKA, H. *Science*, 1945, **101**, 695; ESPOY, H. M. *Science*, 1946, **103**, 175; SMITH, E. L. *Science*, 1946, **103**, 281.
4. WILKIE, J. B., and DEWITT, J. B. *J. Ass. off. agric. Chem.*, 1945, **28**, 174.

Letters to the Editor

Life Insurance Medical Research Fund Grants

On page 392 of *Science* for 25 October 1946, in an announcement of grants made by the Life Insurance Medical Research Fund, it was incorrectly stated that grants recently made in support of medical research at the Carnegie Institution of Washington, McGill University, and New York University had a total value of $633,591. This amount, $633,591, in fact represents the total value of all grants-in-aid made by the Life Insurance Medical Research Fund since its inception a year ago. In addition to this sum, fellowships with a total value of $55,800 have been awarded by this Fund in 1946.

FRANCIS R. DIEUAIDE
Life Insurance Medical Research Fund, New York City

Myosin and Adenosinetriphosphatase in Muscular Activity

It is now generally assumed that the hydrolytic splitting of ATP furnishes the energy for muscular contraction or relaxation, and that this splitting is catalyzed by the contractile protein, myosin, itself, or by an enzyme closely associated with it.

Evidence obtained from recent experiments in this laboratory does not support this view.

It is found that the enzymatic activity of myosin or actomyosin, even under optimal conditions, is strongly inhibited by Mg-ions, and it can be shown that in muscle this inhibition is probably fully developed. Calculations show that the liberation of inorganic phosphate from ATP by myosin in dog muscle can take place with a speed of, at most, 0.003 mg. P/minute/mg. myosin.

From data in the literature (E. Lundsgaard. *Biochem. Z.*, 1930, **227**, 51), on the other hand, it is calculated that the liberation of inorganic phosphate in contracting frog muscle takes place at a rate of at least 0.200 mg. P/minute/mg. myosin. Therefore, it is concluded that hydrolysis of ATP by myosin—ATPase— cannot be the source of the liberated inorganic P and of the energy for muscular activity.

On the other hand, it is found that ATP induces striking physical changes in myosin even under conditions which exclude hydrolysis of the ATP. It is not denied, therefore, that interactions between ATP and myosin (and ions) form the basic phenomena of muscular activity.

Detailed publications will be submitted to the *Journal of General Physiology*.

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The Possible Role of the Guppy, *Lebistes reticulatus*, on the Biological Control of *Schistosomiasis mansoni*

It has been observed that, in certain regions in Puerto Rico endemic for schistosomiasis and where numerous snails (*Australorbis glabratus*) could be recovered previously, these can no longer be found. Instead, numerous guppies of the species, *Lebistes reticulatus* (Peters), are seen in the water. Some of these were collected and brought to the laboratory. When placed in aquariums and other artificial containers, the guppies fed actively on the egg masses laid by the snails on rocks inside the aquariums, along the sides of the glass containers, on the vegetation, and on the snails' own shells. The fish preferred to attack those egg masses containing young snails just about ready to come out. On another experiment it was also observed that the guppies fed readily on cercariae shed by the snails.

According to S. D. Erdman in "Aquarium fishes in Puerto Rico" (*Rev. Agric. P.R.*, in press), *A. glabratus* is common where guppies are found. This investigator suggests that the absence of guppies in certain aquatic regions in Puerto Rico may be due to the fact that the *A. glabratus* is also absent. The egg masses of the snail may constitute essential food for the guppy for which the fish might have predilection.

Further investigations on this problem are being carried on. Guppies have been introduced in bodies of water containing snails, and the effect on the snail population is being constantly observed.

The author wishes to express his gratitude to B. Quiñonez Chacón and Felix Iñigo, from the Division of Fisheries, Department of Agriculture and Commerce, for the identification of the guppy and for their cooperation in this work.

JOSÉ OLIVER-GONZÁLEZ
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Reduction of Excess Acetylcholine in the Serum of Pernicious Anemia Patients by Treatment With Pteroyl Glutamic Acid, Liver Extract, or Ventriculin

Continued, twice-daily injections of acetylcholine into dogs was shown by us (*Science*, 1946, **104**, 37) to produce a hyperchromic anemia which responds to treatment with pteroyl glutamic acid or liver extract. Evidence was also presented which indicated that the therapeutic agents employed for producing remission of certain macrocytic anemias acted by increasing the cholinesterase activity of the organism. This letter is written to report some recently obtained observations on human patients with well-established diagnoses of pernicious anemia.

Serum acetylcholine concentrations were estimated on three patients in relapse and two patients in therapeutic remission. Our method of determining serum acetylcholine is being published elsewhere. It involves a biological assay utilizing the eserinized rectus abdominis muscle of the frog. In one case, the identification of the active substance in the serum as acetylcholine was made more certain by an experiment in which it was observed to cause a contraction of an isolated segment of rabbit intestine which was subsequently antagonized by atropine.

It was found that three pernicious anemia patients

in relapse had serum acetylcholine concentrations varying from 15 to 18 γ/100 cc. of serum. On the seventh or eighth day of treatment, when reticulocyte responses were near their peaks, each of the three patients was found to have about 6.5 γ of acetylcholine/100 cc. of serum. Two normal human subjects also had about 6.5 γ per cent in their sera, while two patients with pernicious anemia in remission, upon returning for maintenance treatment with liver, were found to have 8 and 10 γ per cent of acetylcholine.

Each of the three cases of pernicious anemia in relapse was treated with a different therapeutic agent or preparation. One patient, severely ill, received 60 mg. of pteroyl glutamic acid intramuscularly per day; one received 40 grams of ventriculin daily; and one received 1 unit of liver extract, intramuscularly, per day. As a chemical result of these varied treatments, all three patients showed a reduction of approximately 60 per cent from their high serum acetylcholine levels.

A study of the serum cholinesterase will be reported later, but to date we have found that this activity *is* present in the serum of pernicious anemia patients during relapse, and is, in general, proportional to the erythrocyte count.

These experiments were performed in Detroit, Michigan. Grateful appreciation is expressed to the Anemia Laboratory of Parke, Davis and Company, and its director, Dr. E. A. Sharp, who made these cases available; to Drs. E. C. Vonder Heide, L. Berman, and Axelrod, who diagnosed and treated these cases; and to Dr. W. H. Seegers and the Department of Physiology, Wayne University, for the use of laboratory space and facilities.

JOHN EMERSON DAVIS
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On Virus Nomenclature

The chaotic state of virus nomenclature needs little elaboration. It is apparent that, with no rules to follow, a whim may result in the designation of a new agent after a variety of entities—a host, a geographical location, a disease condition, a season of the year, or the discoverer thus forming a simple nomial or very involved polynomials. Unwieldy names like *Eastern-Russian-spring-summer encephalitis virus* now burden the worker, but even worse is the wealth of synonyms, often only the result of variation in word order, that are used for some virus agents.

This confusion is more likely to increase than decrease with time, since taxonomic classification may be a long way off, while newly discovered viruses continue to be reported in current publications.

A suggestion is offered here that might alleviate some of the confusion in the naming of new viruses by adapting systematically certain current practices, namely, the use of a trinomial such as *Equine encephalomyelitis* (*Eastern*) or *Mouse pneumonitis* (*Nigg*)—a system which has several points to recommend it. The first name indicates the apparent primary host; the second, the type of disease; and the third, the immunological strain, after the isolator or the region where it was recovered. If a number of virus agents were named in this manner, it would not be necessary to affix the word *virus* to the name, as that connotation would be carried by the form itself. At any rate, the agent would have a somewhat descriptive and rather precise name considerably easier to handle in writing and in speaking than one like *submaxillary gland virus of guinea pigs*, which may be written *guinea pig submaxillary gland disease* and another time *virus disease of the submaxillary gland of guinea pigs*—a variability that causes some difficulty when searching the literature and which might have been avoided by a trinomial like *Cavian submaxillitis* (*C. & K.*).

However, this suggestion is offered not with the intention of altering well-established names but as a basis for reconsidering the current practices of coining names for virus agents.

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Book Reviews

Scientists against time. James Phinney Baxter, 3rd. Boston: Little, Brown, 1946. Pp. xv + 473. (Illustrated.) $5.00.

This is a book for which American scientists have been waiting. It tells the official story of the Office of Scientific Research and Development. Within the limits of one volume it presents a clear, detailed, and yet stylistically most attractive account of the victory made possible by the civilian scientific research effort of our Nation during World War II.

The author, James Phinney Baxter, 3rd, is president of Williams College and a former professor of history at Harvard. His special field of distinction in historical scholarship has included the consideration of the effect of the introduction of new weapons, such as the ironclad warship, in previous wars. His selection as official historian of OSRD was therefore most fortunate. The present book is not to be mentioned in the same breath with the drab and desiccated bureaucratic documents that are sometimes issued by Federal agencies as the story of the past.

Dr. Vannevar Bush, the director of OSRD, says in his foreword that the book is "the history of a rapid transition, from warfare as it has been waged for thousands of years by the direct clash of hordes of armed men, to a new type of warfare in which science becomes applied to

destruction on a wholesale basis. It marks, therefore, a turning point in the broad history of civilization.''

On 27 June 1940, the National Defense Research Committee, the parent organization of OSRD, was created by President Roosevelt, with Vannevar Bush, president of the Carnegie Institution of Washington, as its chairman. The other initial members of the Committee were Frank B. Jewett, president of the National Academy of Sciences, and Conway P. Coe, Commissioner of Patents, both *ex officio*; President James B. Conant, of Harvard; President Karl T. Compton, of the Massachusetts Institute of Technology; Dr. R. C. Tolman, of the California Institute of Technology; and an official representative each of the Army and the Navy.

From the first, Bush delegated responsibility to division heads, named from among the members of the Committee. He also early set the plan of operation of OSRD by directing that, instead of starting vast new Federal research organizations, the pattern rather was to be that of granting research contracts to universities, colleges, and industrial research laboratories for the study of specific problems.

Every American scientist now knows of the success of this policy. England, with a much simpler problem of the mobilization of scientific work, was also successful, but our enemies failed in their effort to bring civilian scientific brains effectively to the service of their nations at war. Prof. William Osenberg, who attempted the mobilization of German civilian scientists, said just before the surrender of his nation: ''Germany lost the war because of incomplete mobilization and utilization of scientific brains.'' A similar unfavorable statement can be made in regard to the use of civilian scientists in Japan.

The present volume is divided into six parts, as follows: 1, ''The Race for Superiority in New Weapons in the Second World War''; 2, ''New Weapons and Devices''; 3, ''Chemistry and the War''; 4, ''Military Medicine''; 5, ''Men and Machines''; and 6, ''The Atomic Bomb.''

The space allotted to this review does not allow a summary or critique of these sections. It may be pointed out, however, that the CMR (Committee on Medical Research) of OSRD, under the chairmanship of Dr. A. N. Richards, of the University of Pennsylvania, developed many procedures which were not only basic to war but are also of very great importance in peace. Similarly, many of the other scientific advances described in each section of the book have an important bearing upon the problems of our peacetime economy. This is especially true of some of the work done by psychologists under OSRD contracts in the development of new techniques of selection and training.

The final climactic section of the book summarizes in brief compass the great adventure of the utilization of atomic energy in warfare. In thinking of this achievement one must never forget that no one has yet successfully challenged the estimate that the atomic bomb, by forcing the surrender of Japan while its armies were still intact, may well have saved the lives of 1,000,000 American and 250,000 British fighting men.

This review can best close by quoting some of Baxter's wise observations upon the implication for the future of this development of atomic energy as an instrument of warfare:

''At the close of earlier wars, sensible men and women have demanded that international anarchy be supplanted by international organization and that swords be turned into plowshares. But the good resolutions of the morning after have not yet become the basis of durable peace. . . .

''Until the world creates an international organization strong enough to control the genie who escaped from his bottle at Alamogordo, we must keep our powder dry. . . .

''What we need is military strength without militarism and realistic advancement of the structure of world peace without the self-deception to which pacifists are liable.''

It will be difficult for anyone to read this book and not become an advocate of a strong, federally supported science organization to continue the research necessary for our future military preparedness and for the solution of basic peacetime problems as well.

LEONARD CARMICHAEL
Tufts College, Medford, Massachusetts

Encyclopedia of hydrocarbon compounds, C_1 to C_5. Joseph E. Faraday. (Compiler.) Brooklyn, N. Y.: Chemical Publishing Co., 1946. $15.00.

In the foreword of this book the author writes as follows:

''In the literature of Organic Chemistry there are two comprehensive works that detail every compound known, identified and analyzed up to a certain date. These are 'Richter's Lexicon der Kohlenstaff Verbindungen' and 'Beilstein's Handbuch der Organischen Chemie.' They suffer from the great disadvantage that they are decades out-of-date, from the minor drawback that they are in German, and in the case of Beilstein, from a very complicated system of arrangement.

''The Encyclopedia of Hydrocarbon Compounds overcomes these disadvantages. The arrangement as a loose leaf system allows it to be kept permanently up-to-date by the issue of regular supplements of sheets to be inserted in their appropriate places. The system of arrangement of the compounds is the formula index system of Richter, one of the simplest possible.

''The source of all information up to January 1, 1919, has been Beilstein's Handbuch der Organischen Chemie, the main work and the first supplement. . . . The sources of information from January 1, 1919, to the present day have been the three great abstract journals of Chemistry, namely British Chemical Abstracts, Chemical Abstracts and Chemisches Zentralblatt. . . .''

The following information is presented in the case of each compound, where available: molecular formula, expanded structural formula, names, occurrence, known methods of preparation (with references), melting and freezing point, boiling point, density, and solubility in organic solvents.

Supplements are planned to be issued yearly, on two types of sheets, one for new compounds and one for additions.

The system of arrangement is that of "Richter's Lexicon der Kohlenstaff Verbindungen" in so far as it applies to compounds of carbon and hydrogen only. The elements are given in the order: C, H, D, T. The last two symbols represent the deuterium and tritium isotopes of hydrogen.

The compounds are arranged first into classes according to the number of carbon atoms in the molecule, and second into groups within each class according to the number of hydrogen atoms. Deuterium and tritium compounds are placed immediately before the corresponding all H^1 compound in order of the number of deuterium or tritium atoms, the largest coming first, e.g. CD_4, CHD_3, CH_2D_2, CH_3D, CH_4.

Compounds of the same molecular formula are arranged further according to the degree of unsaturation, with saturated compounds first. A double bond is one degree of unsaturation; a triple bond, two degrees. These compounds are then arranged according to the occurrence of double and triple bonds. Two double bonds precede a triple bond. The aromatic nucleus is regarded as saturated. Still further arrangements include those according to the longest straight chain or largest cyclic system of carbon atoms, the greatest coming first, and those according to the length of the largest substituent group, the smallest coming first, e.g. two methyl substituents precede an ethyl substituent.

The system of nomenclature follows very closely the "International rules for naming organic compounds" (*J. Amer. chem. Soc.*, 1933, 55, 3905).

A total of 554 references are given to the preparation of methane, 66 for n-pentane, 70 for isopentane, and 13 for neopentane. Similar relatively large numbers of references are given for the preparation of the other compounds.

The summaries of physical properties are only of very general value because of their incompleteness and noncritical selection of data.

The encyclopedia will be useful mainly to organic chemists interested in the synthesis of these hydrocarbons and to physical and petroleum chemists interested in reactions involving these compounds.

This book is recommended to those interested in finding recorded in one place references to substantially all the published methods of preparation of these hydrocarbons.

FREDERICK D. ROSSINI
National Bureau of Standards, Washington, D. C.

Genera et species plantarum argentinarum. **(Vol. 1.) (Ed. by National University of Tucumán.) Buenos Aires: Fundacion Miguel Lillo, 1943. Pp. xxi + 331. (Illustrated.) 160 pesos.**

During recent years there has been an ever-increasing output of botanical studies from the city of Tucumán, situated near the base of the Andes in northwestern Argentina. This has been quickened by the foundation, a decade ago, of the Botanical Institute that bears the name of Tucumán's distinguished botanist, Miguel Lillo (1862–1931). The journal *Lilloa*, initiated in 1937, has shown a rapid development in the number and quality of its botanical papers and a corresponding excellence in the technique of its printing and illustrations. Now we welcome from the Instituto Botanico one of the most sumptuous volumes, as to format, printing, and illustrations, that has ever been produced in the New World; in these matters it compares with the royally supported expedition reports of a century ago rather than with the usual scientific papers of our time.

The work, bound in heavy, light green cloth, is a folio of 331 pages, its firm sheets measuring 34 × 50 cm. Its first pages give dedications to various persons, some of whom are public officers and others those in authority at the University and the Institute in Tucumán. The last page tells in some detail of the mechanical production of this volume, recording those in charge of each stage of the processes of printing and engraving and stating the size of the edition which has been both directly printed on special paper and reproduced by an offset method.

The actual text of the book, which employs both Spanish and Latin, contains accounts of three families of flowering plants. To these are added "Icones Plantarum Argentinarum," a series of 11 beautiful paintings of miscellaneous flowering plants, unaccompanied by descriptive text. The three families considered are illustrated by similar plates, except that only a small proportion of them are colored. Of these families the Zygophyllaceae, with text prepared by H. R. Descole, C. A. O'Donell, and A. Lourteig, contain 7 genera and 16 species, each specially treated and mapped; the Cactaceae, by A. Castellanos and H. Lelong, comprise 26 genera duly distinguished on an analytical key, but there is no consideration of individual species; while the Euphorbiaceae, by A. Lourteig and C. A. O'Donell, are elaborated with a key to the 25 genera as well as keys to the species of all except those of the large genera, *Croton*, *Julocroton*, and *Euphorbia*. Ninety-five such species are considered.

The current numbers of *Lilloa* carry papers of a more technical nature that supplement the accounts of special families under consideration. The above authors have thus treated the Zygophyllaceae (*Lilloa*, 1940, 5, 257–352) and the Euphorbiaceae (*Lilloa*, 1943, 9, 77–177), with special discussions, ample citation of specimens studied, etc. Perhaps a similar additional account of Cactaceae is forthcoming, or perhaps this family is to rest for the present on the classic work of Britton and Rose.

It is the merit of the plates, and especially the beauty of those in color, that will constitute the permanent value of this work. If the project should be carried to fulfillment, this is merely the first of many such volumes. The whole will constitute a magnificent presentation of the Argentine flora.

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